THE UNIVERSITY OF ALBERTA

THE PHOTOLYSIS OF METHYL 6-DEOXY-6-IODO-α-D-GLUCOPYRANOSIDE IN AQUEOUS MEDIA

BY

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled,

THE PHOTOLYSIS OF METHYL 6-DEOXY-6-IODO-
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submitted by Bruce A. Graham, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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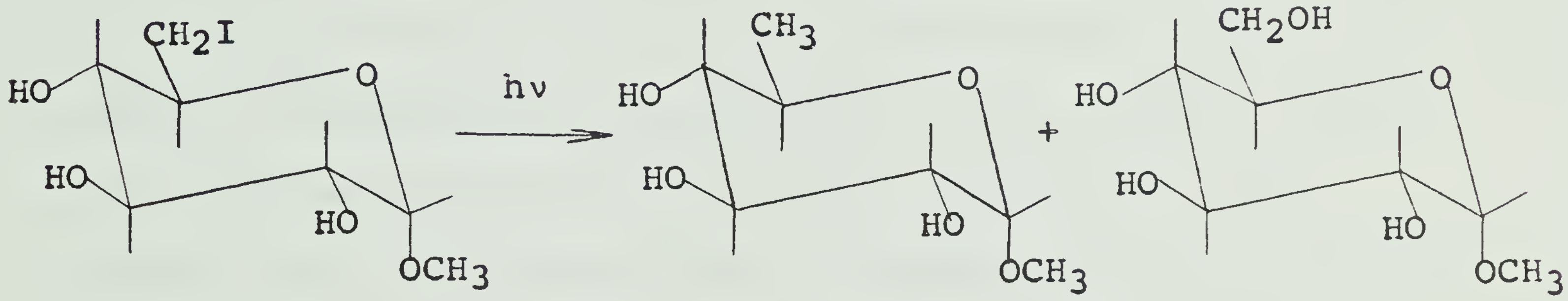
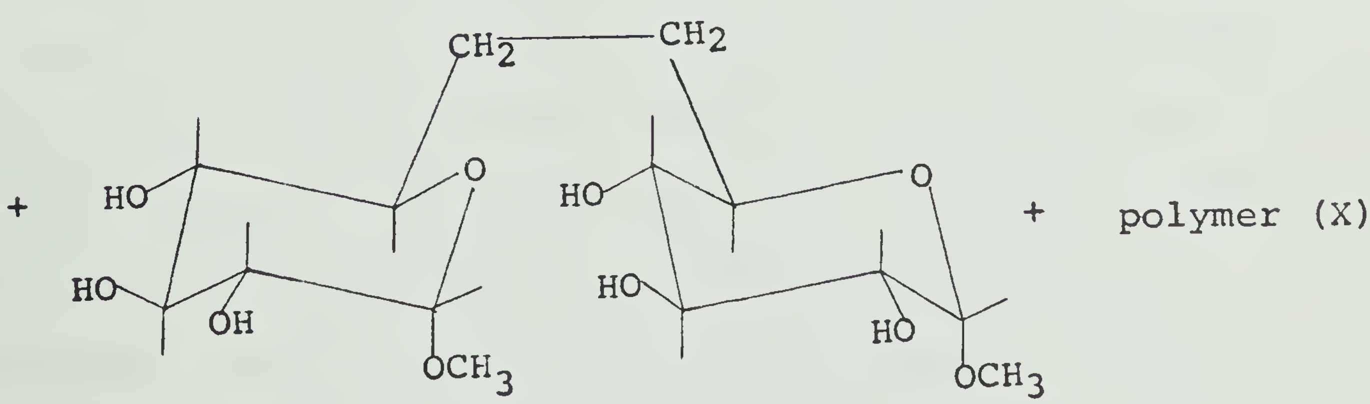
ABSTRACT

The reactions of the methyl 6-deoxy-α-D-gluco-pyranoside radical (II), generated in sodium bicarbonate-buffered aqueous media by irradiating a solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I) with ultraviolet light, were investigated. In a typical experiment, a 0.12 M solution of I produced methyl 6-deoxy-α-D-glucopyranoside (III) (23%), methyl α-D-glucopyranoside (3.5%), methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside (V) (6%) and products (X) (about 30%) which appeared to have been formed from three or more molecules of methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I).



I

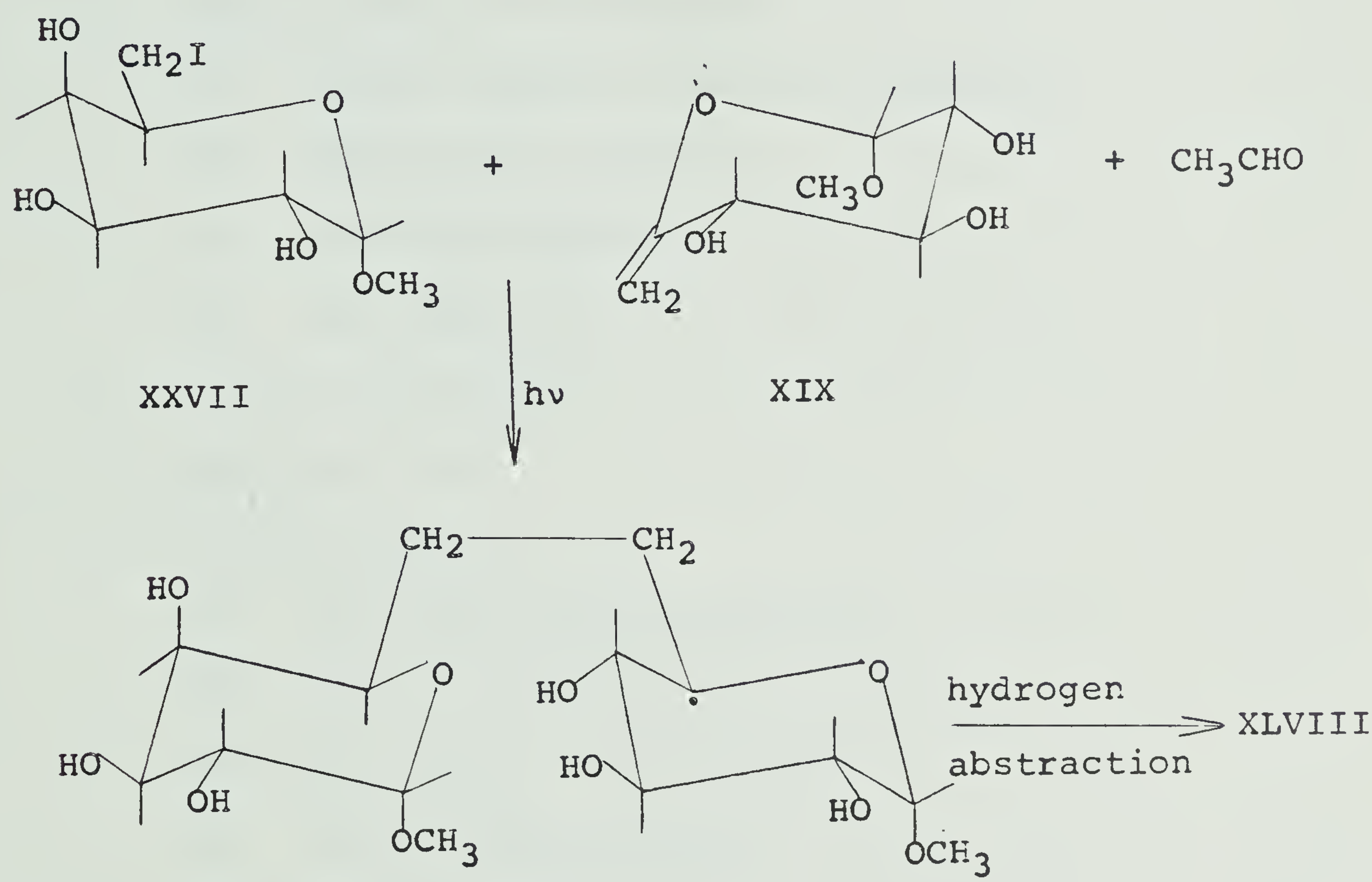
III



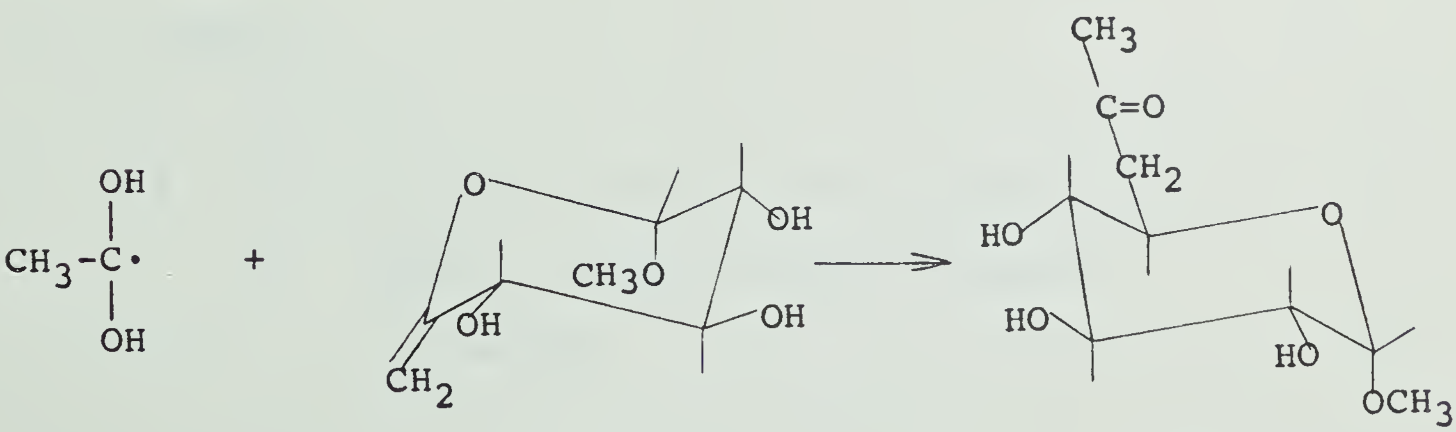
V

The dimer (V) was not formed to an appreciable extent by the coupling of radicals (II) since it could not be detected until at least 25% of I had undergone photolysis. Methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside (XIX) was thus indicated as a required intermediate although this compound could not be detected in the course of the reaction. To test this hypothesis, methyl 6-deoxy-6-iodo-α-D-galactopyranoside (XXVII) was photolysed in the presence of XIX and a source of hydrogen atoms (a 100 molar excess of acetaldehyde). The dimer expected from the coupling of methyl 6-deoxy-α-D-galactopyranoside radicals, which formed on photolysis of XXVII in the absence of XIX, could not be detected. Instead, methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-glucopyranoside (XLVIII) was formed, as expected, by the addition of the methyl 6-deoxy-α-D-galactopyranoside radical to XIX to form the dimer radical XLIX which abstracted a hydrogen atom to form XLVIII. The vinyl ether XIX is therefore indicated as a required intermediate for the formation of V. The polymeric products X may have arisen in a similar manner through the formation of vinyl ethers from the dimer radical or by addition of the dimer radical to the vinyl ether XIX, etc. When I was photolysed in the presence of the same concentration of acetaldehyde no dimer was formed and only methyl 6-deoxy-α-D-glucopyranoside (III) (80%) and methyl 6,8-dideoxy-α-D-gluco-octopyranoside (XXV) (6%) were detected as products

of the reaction. The photolysis of either of the iodides, I or XXVII, in the presence of equimolar amounts of the vinyl ether XIX led to the formation of methyl 6,8-dideoxy-α-D-gluco-octopyranosid-7-ulose (XLV) (∿35%). Addition of the methyl 6-deoxy-α-D-glucopyranoside radical (II) to formaldehyde to give methyl 6-deoxy-α-D-gluco-heptopyranoside (XXI) (10%) was also demonstrated.



XLIX



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INTRODUCTION

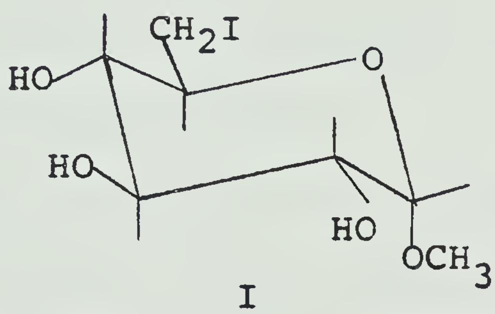
Photochemically induced reactions have only recently been applied to syntheses in carbohydrate chemistry, in fact most of these have appeared in the course of the present research. In 1966 Horton and Jewell (1) irradiated a solution of D-galactose diethyl dithioacetal in methanol to obtain 1-S-ethyl-1-thio-D-galactitol which on further irradiation yielded 1-deoxy-D-galactitol. Each step in this reaction involves cleavage of a carbon-sulfur bond by absorption of light, followed by hydrogen abstraction by the carbohydrate radical formed. Lehmann (2) found that the toluene-α-thiol radical added to carbohydrates containing a double bond, for example, the toluene-α-thiol radical was added to methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside to give methyl 6-S-benzyl-6-thio-α-D-glucopyranoside. More recently Whistler (3) demonstrated the possibility of forming carbon-phosphorus bonds in carbohydrates by the UV irradiation of 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose with phosphine to give 5,6-deoxy-1,2-*O*-isopropylidene-6-phosphine-α-D-glucofuranose and bis-(5,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose-6-) phosphine.

A comprehensive review of the effect of ultraviolet light on aqueous solutions of carbohydrates has recently been published by Phillips (4). He concludes that although the evidence is often contradictory, it appears that, in general terms: a) monosaccharides are degraded, by way of

acids and fragments containing fewer carbon atoms, to carbon dioxide; b) the glycosidic link is susceptible to cleavage by light; c) polysaccharides are depolymerized; and d) the final product is carbon dioxide. Although during the last sixty years extensive work has been done on the effect of light on carbohydrates, insufficient attention has been paid to such photochemical variables as wavelength of the light used, the presence of photosensitizers, and the presence of oxygen, to enable one to say whether direct photolysis of a carbohydrate containing no obvious absorbing groups occurs in aqueous solutions when radiation of wavelengths greater than 2000 Å is applied.

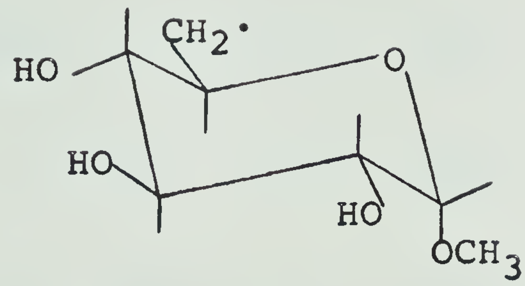
It was apparent that the liberation of carbon radicals from carbohydrate molecules and their engagement with radical acceptors would open routes to new carbohydrate structures. To enable reactions of the carbohydrate radicals with added solutes to be promoted it was decided to liberate the radicals in aqueous media since water was not expected to serve as a hydrogen-atom donor. In particular the reaction of carbohydrate radicals with alkenes and aldehydes seemed of interest. However, very little information was available on the properties of carbohydrate radicals and, as a consequence, it was necessary in the first stages of this investigation to produce carbohydrate radicals and to examine the course of their reactions in the absence of possible radical acceptors. Indeed, as will be seen, this study formed the major portion of this investigation.

Of the several possible methods of producing carbohydrate radicals in aqueous media, the irradiation of deoxyiodoglycosides seemed most attractive because of their ease of preparation. Although a wide variety of both primary and secondary deoxyiodoglycosides are readily available, it was decided to begin the investigation in this area by examining the most readily available of such compounds; namely, methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I) (5).



I

The ultraviolet absorption spectra of primary alkyl iodides are characterised by a maximum at 257 mμ (ε 400 - 500) (6) due to the excitation (n→σ*) of a non bonded iodine 5p electron into the lowest empty anti-bonding σ-orbital of the carbon-iodine bond (7). Iredale (8) in 1929 showed that the photochemical decomposition of ethyl iodide was the result of the absorption of one quantum of light, causing the detachment of an iodine atom. Thus, the irradiation of I would produce, initially, the radical II. This research is concerned with



II

the reactions of both this radical and the analogous radical with the *galacto* configuration.

In 1931 Emschwiller (9, 10) observed that the decomposition of simple alkyl iodides by light resulted in a yield of approximately equal amounts of alkane and alkene. In 1951 Hamill and Schuler (11) suggested that the observation of approximately equal yields of ethane and ethylene in the photolysis of liquid ethyl iodide required a mechanism involving the reaction of a "hot" ethyl radical with an ethyl iodide molecule to give a molecule of ethane and a molecule of ethylene.

$$C_2H_5\cdot \quad + \quad C_2H_5I \longrightarrow C_2H_6 \quad + \quad \cdot C_2H_4I$$

$$\cdot C_2H_4I \longrightarrow C_2H_4 \quad + \quad I\cdot$$

McCauley, Hamill and Williams (12) in 1954 proposed a similar "hot" radical mechanism to account for the formation of propane and propylene in the photolysis of liquid n-propyl

iodide. The small quantity of ethylene produced in the reaction was explained by a β-scission reaction:

$$CH_3CH_2CH_2\cdot \longrightarrow CH_3\cdot + CH_2{=}CH_2$$

$$CH_3\cdot + I_2 \longrightarrow CH_3I + I\cdot$$

This mechanism was supported by the discovery of appropriate quantities of methyl iodide. The identification of considerable quantities of isopropyl iodide in the product was explained by suggesting the production of HI during the reaction:

$$CH_3CH_2CH_2I + h\nu \longrightarrow CH_3CH{=}CH_2 + HI$$

$$CH_3CH{=}CH_2 + I\cdot \longrightarrow CH_3CHICH_2\cdot$$

$$CH_3CHICH_2\cdot + I_2 \longrightarrow CH_3CHICH_2I + I\cdot$$

$$CH_3CHICH_2\cdot + HI \longrightarrow CH_3CHICH_3 + I\cdot$$

The authors do not appear to have considered the possibility that the isopropyl iodide arose from the ionic addition of hydrogen iodide to propylene.

In 1956 Bunbury, Williams and Hamill (13) showed that in the photolysis of liquid ethyl iodide virtually all the ethane produced was due to the reaction of ethyl radicals with hydrogen iodide:

$$C_2H_5\cdot + HI \longrightarrow C_2H_6 + I\cdot$$

Only a small contribution arose from a "hot" radical reaction. They explained the production of HI by postulating a "diffusion-controlled disproportionation":

$$C_2H_5I \;+\; h\nu \;\longrightarrow\; (C_2H_5\cdot \;+\; I\cdot)$$

$$(C_2H_5\cdot \;+\; I\cdot) \;\longrightarrow\; C_2H_4 \;+\; HI$$

Also, they showed that a substantial part of the ethane produced on photolysis of a solution of ethyl iodide in cyclohexane does not arise from reaction with hydrogen iodide but instead by abstraction of a hydrogen atom from the cyclohexane. No significant amount of "dimer" due to the combination of two alkyl radicals was found in any of these experiments.

In contrast to the experiments described above which involved the photolysis of small, poorly solvated alkyl iodide molecules, either pure or dissolved in organic solvents, the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside involves a bulky molecule strongly solvated in aqueous media. The effect of the stereochemistry of the bulky solvated molecule on the course of reactions, such as hydrogen abstraction by a radical, was expected to be significant.

Kharasch and Goethlich (14) have photolysed solutions of iodoaromatic compounds in benzene and have observed the following types of reactions:

$$C_6H_5C{\equiv}CI \quad + \quad h\nu \xrightarrow{C_6H_6} (C_6H_5C{\equiv}C-)_2$$

$$pIC_6H_4CHO \quad + \quad h\nu \xrightarrow{C_6H_6} pC_6H_5C_6H_4CHO$$

This latter reaction, addition of a radical to the benzene solvent, has been used synthetically by Nickon and Aaronoff (15). Kupchan and Wormser (16) studied the intramolecular application of this reaction by photolysing 2-iodo-stilbenes to give phenanthrene derivatives. In this way they synthesised aristolochic acid. Wolf and Kharasch (17) have further investigated the photolysis of iodoaromatic compounds as a method of arylating benzene.

Kharasch and Friedman (18) have shown how the photolysis of iodoaromatic compounds in a solvent such as methanol can be used to replace the iodine by hydrogen. They suggest the following mechanism to explain their results:

$$ArI \quad + \quad h\nu \longrightarrow I\cdot \quad + \quad Ar\cdot$$

$$Ar\cdot \quad + \quad CH_3OH \longrightarrow ArH \quad + \quad \cdot CH_2OH$$

$$\cdot CH_2OH \quad + \quad I\cdot \longrightarrow ICH_2OH \longrightarrow HI \quad + \quad H_2CO$$

$$H_2CO \quad + \quad 2CH_3OH \longrightarrow H_2C(OCH_3)_2$$

$$CH_3OH \quad + \quad HI \longrightarrow CH_3I \quad + \quad H_2O$$

EXPERIMENTAL

I. METHODS

1. Spectroscopic Measurements

(a) Proton magnetic resonance (p.m.r.) spectra were determined using a Varian A60 Spectrometer (60 Mc.p.s.) and a Varian HR 100 Spectrometer (100 Mc.p.s.). Tetramethylsilane (TMS) was used as an internal standard in all solvents except deuterium oxide, where tetramethylsilane was used as an external standard. Chemical shifts are reported in tau (τ) values with respect to the tetramethylsilane standard. Decoupling experiments were conducted using the frequency sweep method. Couplings marked with an asterisk were shown by decoupling experiments.

(b) Ultraviolet (U.V.) spectra were recorded using a Perkin-Elmer (Model 202) Ultraviolet-Visible Spectrometer.

(c) Infra-red (I.R.) spectra were recorded using a Perkin-Elmer (Model 421) Dual Grating Spectrometer.

(d) Mass spectra were determined using an AEI MS9 Mass Spectrometer with an inlet temperature of 185°. Trimethylsilyl ether derivatives were prepared using the procedure of Golding *et al* (19).

2. Optical Rotations.- Optical rotations were measured with a Perkin-Elmer Model 141 Polarimeter.

3. Melting Points.- Melting points were determined on a Leitz Microscope Heating Stage (Model 350) and are uncorrected.

4. Chromatography

(a) Gas-liquid chromatography (g.l.c.) was performed with an F and M (Model 500) Gas Chromatograph using helium as the carrier gas. O-Acetyl derivatives were chromatographed using a column (8' x 1/4") packed with a mixture of 5% diethylene glycol adipate and 3% SE-52 on Chromosorb W (not acid-washed). O-Trimethylsilyl derivatives were chromatographed using a column (8' x 1/4") packed with 3% SE-30 on Chromosorb W (not acid-washed).

(b) Paper chromatograms were done on Whatman No. 1 paper. Solvent systems used were the less dense phase of equilibrated n-butanol, ethanol, water (5:1:4, by vol.) (20), and n-butanol, pyridine, acetic acid, water (6:4:1:3, by vol.). In the text these systems are referred to as solvent systems A and B respectively. Spray reagents used to detect compounds on the chromatograms were alkaline silver nitrate (21) and permanganate-periodate (22).

(c) Thin-layer chromatograms (t.l.c.).- Silica gel G thin layer chromatograms were viewed by spraying the plates with 33% sulfuric acid and heating on a hot plate. Microcrystalline cellulose t.l.c. plates were examined by dipping them in a solution of silver nitrate in acetone and, after drying, spraying them with a solution of sodium hydroxide in ethanol.

(d) Preparative chromatography was done on columns, the fractions being collected by means of a mechanical fraction collector. Individual fractions were examined by one or more

of the following methods: paper chromatography, t.l.c., optical rotation, and concentration in vacuo with weighing of the residue.

(i) Celite columns were prepared using the method of Lemieux (23). In all cases the solvent system used was equilibrated n-butanol-water. An equal weight of the denser phase was absorbed onto the Celite support and the column was eluted with the less dense phase.

(ii) Charcoal columns (400 x 55 mm) were prepared using the method of Whistler (24) and compounds were eluted from the column by gradient elution with ethanol-water. The column was set up for gradient elution by connecting in series, by a syphon, two erlenmeyer flasks (2 l), one of which contained water (2 l) and the other 1/2% (v/v) ethanol in water (2 l). To ensure complete mixing of the solution a magnetic stirring bar was placed in the flask containing water, from which the solution was pumped to the top of the column using a Watson-Marlow H. R. Flow-inducer, type MHRE. When the two flasks were empty they were refilled with 1/2% (v/v) ethanol-water and 1% (v/v) ethanol-water so that the strength of the ethanol solution increased smoothly. Further increases of 2, 4, 8, 16, 25% (v/v) ethanol-water were made in the same way.

(iii) Microcrystalline cellulose columns were prepared using the method of Wolfrom (25). In all cases the eluent used was the less dense phase of equilibrated n-butanol, ethanol, water (5:1:4, by vol.).

5. Acetylations

Acetylations were done by dissolving the compound in pyridine, adding excess acetic anhydride, and allowing the mixture to stand for approximately sixteen hours at room temperature. Unless otherwise stated the reaction mixture was worked up by pouring it into water and extracting into chloroform; the chloroform extract being washed consecutively with 10% sulfuric acid, saturated sodium bicarbonate and water before being dried over anhydrous sodium sulfate. The chloroform solution was concentrated *in vacuo* to obtain the product.

II. REAGENTS

1. Solvents

Solvents used were commercially available and, when necessary, were dried using established procedures.

2. Derivatives of Methyl α-D-Glucopyranoside

(a) Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I).- Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside was prepared by the method of Compton (26) from methyl α-D-glucopyranoside. The physical constants (m.p. 148.5 - 149.5°, $[\alpha]_D^{25}$ + 114° (*c*, 3.4 in chloroform), λ_{max}^{MeOH} 255 mμ (ε 428)) were in good agreement with those obtained by Compton: m.p. 149 - 150°, $[\alpha]_D$ +113.8° (*c*, 3.7 in chloroform). The p.m.r. spectrum of methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside in deuteriochloroform is shown in Fig. 2. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside (14.54 g, 33.8 mmole)

was dissolved in methanol (400 ml) containing triethylamine (20 ml) and water (50 ml) was added. After twenty-four hr at room temperature the solution was concentrated *in vacuo* and the residue was crystallised from ethyl acetate to give methyl 6-deoxy-6-iodo-α-D-glucopyranoside (8.5 g, 28 mmole); m.p. 146 - 148°, $[\alpha]_D^{25}$ +103° (*c*, 4.2 in water), $\lambda_{max}^{H_2O}$ 252 mμ (ε 476). Literature values (5) are $[\alpha]_D^{25}$ +101.5° (*c*, 5.0 in water), m.p. 146 - 147°. The p.m.r. spectrum of methyl 6-deoxy-6-iodo-α-D-glucopyranoside in deuterium oxide is shown in Fig. 3.

Anal. Calcd. for $C_7H_{13}O_5I$: C, 27.64; H, 4.31%; M.W., 304. Found: C, 27.78; H, 4.29%; M.W., 295.

(b) Methyl 6-deoxy-α-D-glucopyranoside (III).- Methyl 6-deoxy-α-D-glucopyranoside was prepared by hydrogenating methyl 6-deoxy-6-iodo-α-D-glucopyranoside using palladium on charcoal as the catalyst to give, on crystallisation from ethyl acetate, a compound, III, with $[\alpha]_D^{25}$ +153.9° (*c*, 2.3 in water), m.p. 97 - 98° (32).

(c) Methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d (XV).- 1,5-D-Gluconolactone (15 g, 90 mmole) was dissolved in ice water (100 ml) in a 600 ml beaker. Sodium borodeuteride (1.27 g, 30 mmole), dissolved in cold water (50 ml), was added dropwise over a period of thirty min to the stirred, cooled lactone solution (71). The acidity of the solution was continuously monitored by means of a pH meter and a pH range of 3.5 - 4.0 was maintained by the addition of 1.0 N sulfuric acid dropwise from a burette. When addition of the sodium borodeuteride solution was complete the solution was allowed to stand for

a further thirty minutes, then passed through a column of Amberlite IR 120 resin (H^+, 50 ml) on top of Amberlite IRA 400 resin (OH^-, 100 ml). The column was eluted with water until the eluate showed no further optical activity. Concentration in vacuo gave a colourless syrup (7.488 g) which was shown to be D-glucose-1-d. Crystallisation of a small amount of the syrup from methanol gave colourless crystals (60 mg), m.p. 147 - 150° both alone and when mixed with an authentic sample of α-D-glucose. The p.m.r. spectrum of the syrup in deuterium oxide showed no peaks corresponding to an anomeric hydrogen. The yield of D-glucose-1-d based on sodium borodeuteride used was 35%, and on D-gluconolactone, 49%. The formation of methyl glycoside from D-glucose-1-d (7.375 g) was achieved by heating a methanolic solution (40 ml) of D-glucose-1-d with Amberlite IR 120 resin (H^+, 2 ml) at reflux temperature for 16 hr (27). A total yield of 6.265 g of methyl α-D-glucopyranoside-1-d (m.p. 166°, $[\alpha]_D^{25}$ +157° (c, 1.0 in water)) was obtained.

To a stirred solution of methyl α-D-glucopyranoside-1-d (4.901 g, 25.2 mmole) in pyridine (75 ml) at 0°, a solution of p-tolylsulfonyl chloride (5.27 g, 27.6 mmole) in pyridine was added dropwise during one hour. The reaction mixture was left at room temperature for sixteen hours before sodium bicarbonate (2.32 g, 27.6 mmole) and water (20 ml) were added to the stirred solution. Concentration in vacuo at 50° left a light brown syrup which was shown by t.l.c. on silica gel G, using solvent system A, to consist of at least two compounds.

Partition of this syrup between chloroform (30 ml) and water (30 ml) followed by extraction of the aqueous layer with chloroform (2 x 30 ml) gave a complete separation of the two compounds. The aqueous layer was deionised by passing it through a column of Amberlite IR 120 resin (H^+, 15 ml) on top of Amberlite IRA 400 resin (OH^-, 15 ml) to give, on concentration *in vacuo*, 1.618 g of syrup which crystallised from methanol to give unchanged methyl α-D-glucopyranoside-1-d (1.010 g); m.p. 166°, $[\alpha]_D^{25}$ +156.9° (*c*, 1.0 in water).

Concentration *in vacuo* of the chloroform layer gave a syrup which was acetylated by dissolving it in pyridine (50 ml) at 0° and adding acetic anhydride (20 ml). The reaction mixture was warmed to room temperature and allowed to stand for sixteen hours. Concentration *in vacuo* gave a brown syrup which was dissolved in chloroform (150 ml) and worked up in the usual manner to give a syrup (9.692 g). The syrup, dissolved in acetone (125 ml), was added to a pressure reaction bottle containing sodium iodide (15 g), the bottle was shaken until the sodium iodide dissolved and then heated at 95° for 1.5 hours. Filtration of the cooled reaction mixture gave crystalline (2.7 g, 13.8 mmole) sodium p-tolylsulfonate. Concentration *in vacuo* of the filtrate left a syrup which was dissolved in chloroform (100 ml), extracted with water (1 x 40 ml) to remove unreacted sodium iodide, dried over anhydrous sodium sulfate and concentrated *in vacuo* to a syrup which crystallised from methanol to give methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside-1-d (4.034 g). Concentration *in vacuo* of the mother liquor gave a syrup

(2.7 g) which when examined by silica gel G t.l.c. using a 3% (v/v) solution of acetone in chloroform, showed the presence of three compounds with R_f values 0.43, 0.54, 0.67. These three compounds were separated by chromatography of the mixture on a column of silicic acid (450 x 30 mm) using chloroform as the eluent. Optical rotations of the 10 ml fractions collected were recorded and in this way three partially resolved peaks could be distinguished. Collection of appropriate fractions gave a complete separation of the three compounds whose R_f values are shown above.

(i) Methyl 3,4-di-*O*-acetyl-6-deoxy-6-iodo-2-*O*-p-tolylsulfonyl-α-D-glucopyranoside-1-d (XXXVII). The first fraction to be eluted from the silicic acid column (R_f value 0.67) gave on concentration a colourless syrup, XXXVII, (0.595 g), $[\alpha]_D^{25}$ +80° (*c*, 2.6 in chloroform), which failed to crystallise. Its p.m.r. spectrum (Fig. 42) showed the following chemical shifts (τ value): H_2, 5.57; H_3, 4.61; H_4, 5.23; H_5, 6.26; $H_{6,6'}$, 6.73 - 6.95; methoxyl, 6.59; p-tolyl-sulfonyl, 2.24, 2.68, 7.53; acetyl, 7.98, 8.22. Coupling constants (c.p.s.) were: $J_{2,3}$, 9.5; $J_{3,4}$, 9.5; $J_{4,5}$, 9.5. Treatment of approximately 10 mg of syrup with 1.0N sodium hydroxide on the steam bath for five minutes followed by acidification with nitric acid and addition of a drop of 1.0 N silver nitrate gave a yellow precipitate typical of silver iodide. A portion of the syrup (0.268 g) was deacetylated by dissolving it in methanol (25 ml) containing triethylamine (1 ml) and adding

water (15 ml) slowly. After forty-eight hours at room temperature the solution was concentrated *in vacuo*; the resulting syrup was dissolved in chloroform (25 ml), extracted with water (10 ml) and the chloroform solution dried with anhydrous sodium sulfate. Concentration *in vacuo* gave a colourless syrup (0.249 g), $[\alpha]_D^{25}$ +70° (*c*, 2.5 in chloroform), which could not be crystallised. The p.m.r. spectrum showed complete deacetylation.

(ii) Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside-1-d (XXXVI). Concentration *in vacuo* of the second fraction eluted from the silicic acid column (R_f value 0.54) gave a colourless syrup (0.485 g) which crystallised on standing and on recrystallisation from methanol was shown to be identical to the first crop of methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside-1-d, XXXVI, $[\alpha]_D^{25}$ +110° (*c*, 1.0 in methanol), m.p. 147 - 148°, both alone and when mixed with an authentic sample of undeuterated compound. The yield of XXXVI, based on the amount of methyl α-D-glucopyranoside-1-d consumed in the reaction was 62%. The p.m.r. spectrum of methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside-1-d (Fig. 43) showed the following chemical shifts (τ value): H_2, 5.15; H_3, 4.54; H_4, 5.14; H_5, 6.2; $H_{6,6'}$, 6.7 - 6.9; methoxyl, 6.52; acetyl, 7.92, 7.93, 7.99. Coupling constants (c.p.s.) were: $J_{2,3}$, 10.0; $J_{3,4}$, 9.0; $J_{4,5}$, 9.0.

(iii) Methyl 3,4,6-tri-*O*-acetyl-2-*O*-p-tolylsulfonyl-α-D-glucopyranoside-1-d (XXXVIII). Concentration of the final

fraction (R_f value 0.43) eluted from the silicic acid column gave a colourless syrup (0.671 g), XXXVIII, which failed to crystallise. Its p.m.r. spectrum (Fig. 44) showed the following chemical shifts (τ value): H_2, 5.56; H_3, 4.59; H_4, 5.05; H_5, 6.1; $H_{6,6'}$, 5.85; methoxyl, 6.62; acetyl, 7.91, 8.01, 8.22; p-tolylsulfonyl, 2.24, 2.68, and 7.53. Coupling constants (c.p.s.) were: $J_{2,3}$, 9.5; $J_{3,4}$, 9.5; $J_{4,5}$, 9.5. The syrup was deacetylated by dissolving it in methanol (25 ml) containing triethylamine (1 ml) and adding water (15 ml) slowly. After reacting for twenty-four hours at room temperature the reaction mixture was concentrated _in vacuo_, and the residue was dissolved in water (10 ml), extracted with chloroform (3 x 25 ml) and the chloroform extract was dried over anhydrous sodium sulfate. Concentration _in vacuo_ of the dry chloroform solution gave a syrup (0.439 g) which was crystallised from n-propanol to give methyl 2-_O_-p-tolylsulfonyl-α-D-glucopyranoside-1-d (231 mg); $[\alpha]_D^{25}$ +82° (_c_, 0.4 in chloroform), m.p. 137 - 139°. The literature (35) values for the undeuterated compound are $[\alpha]_D$ +82.2° (_c_, 2.0 in chloroform), m.p. 139 - 140°.

Methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d (XV) was obtained by dissolving the above 2,3,4-tri-_O_-acetyl compound, XXXVI, in methanol (50 ml) containing triethylamine (2.5 ml) and adding water (50 ml). After sixteen hours, examination by silica gel G t.l.c., using a solution of 3% acetone in chloroform, showed deacetylation was complete and the solution was concentrated _in vacuo_. Crystallisation from ethyl acetate

gave an 86% yield (2.442 g) of XV; $[\alpha]_D^{25}$ +101°, m.p. 145 - 147.5°. The p.m.r. spectrum of methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d, XV, is shown in Fig. 45.

(d) Methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside (XIX).- Methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-xylo-hex-5-enopyranoside ($[\alpha]_D^{25}$ +114.4° (c, 3.2 in chloroform), m.p. 93 - 94°) was prepared by shaking a mixture of silver fluoride (28) and methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside in pyridine as described by Helferich (29). Methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-xylo-hex-5-enopyranoside (10.24 g) was dissolved in a 5% solution of triethylamine in methanol (100 ml) and water (100 ml) was added. After standing for seventeen hr the solution was concentrated in vacuo and an aqueous solution of the residue was passed through a column of Amberlite IRA 400 resin (OH^-, 25 ml) to yield methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside, XIX, (5.7 g) ($[\alpha]_D^{25}$ +96° (c, 4.3 in chloroform)) which crystallised on standing, but could not be recrystallised. The p.m.r. spectrum of XIX in pyridine is shown in Fig. 28.

3. Derivatives of Methyl α-D-Galactopyranoside

(a) Methyl 6-deoxy-6-iodo-α-D-galactopyranoside (XXVII).- Methyl α-D-galactopyranoside monohydrate (58.2 g, 294 mmole), prepared using the procedure of Mills (30), was dissolved in pyridine (200 ml), cooled to 0°, and a solution of p-tolyl-sulfonyl chloride (120.3 g, 630 mmole) in pyridine (250 ml) was added slowly to the stirred solution. After standing at room temperature for eighteen hr the mixture was acetylated with acetic anhydride (200 ml) and worked up in the usual manner

to give a syrup (149 g). A solution of the syrup and sodium iodide (120g) in acetone (500 ml) was heated at 95° for twenty hr before being worked up to give a syrup (138 g). Deacetylation of this syrup (138 g) was accomplished by dissolving it in methanol (500 ml) containing triethylamine (25 g), adding water (300 ml), and allowing the resulting solution to stand at room temperature for forty hr before concentrating it _in vacuo_. Treatment of the residue with water (500 ml) at 100° gave a water-soluble fraction and a water-insoluble fraction. Concentration _in vacuo_ of the water-soluble fraction gave a syrup which crystallised from methanol to give a 23.4% yield of methyl 6-deoxy-6-iodo-α-D-galactopyranoside, XXVII, (21.0 g); $[\alpha]_D^{25}$ +145° (_c_, 1.0 in water), m.p. 169 - 171°, $\lambda_{max}^{H_2O}$ 253 mμ (ε 428). Compound XXVII was shown to contain iodide by heating a solution of 2 mg in 1.0 N sodium hydroxide (1 ml) at 100° for five min before acidifying the solution with dilute nitric acid and adding a few drops of 1.0 N silver nitrate solution to give the yellow precipitate typical of iodides.

Anal. Calcd. for $C_7H_{13}O_5I$: C, 27.64; H, 4.31%. Found: C, 28.05; H, 4.26%.

The p.m.r. spectrum of methyl 6-deoxy-6-iodo-α-D-galactopyranoside (Fig. 45) in deuteriopyridine showed the following chemical shifts (τ value): H_1, 4.94; H_2, 5.51; H_3, 5.72; H_4, approx. 5.6; H_5, 5.84; $H_{6,6'}$, 6.26 - 6.40; methoxyl, 6.54. Coupling constants (c.p.s.) observed were: $J_{1,2}$, 3.25; $J_{2,3}$, 9.75; $J_{3,4}$, 3.0.

(b) Methyl 6-deoxy-6-iodo-3-O-p-tolylsulfonyl-α-D-galactopyranoside (XL).- The water-insoluble fraction from above was acetylated by dissolving it in pyridine (50 ml), adding acetic anhydride (50 ml) and allowing the solution to stand at room temperature for twenty-four hours. Concentration in vacuo at 50° followed by addition of methanol to the syrup gave a crystalline product, which on recrystallising from methanol gave colourless needles (3.3 g) of methyl 2,4-di-O-acetyl-6-deoxy-6-iodo-3-O-p-tolylsulfonyl-α-D-galactopyranoside, XXXIX; $[\alpha]_D^{25}$ +126.8° (c, 1.47 in chloroform) m.p. 201 - 204°, yield 2.1%.

The p.m.r. spectrum of XXXIX (Fig. 46) in deuteriochloroform showed protons with the following chemical shifts (τ value): H_1, H_2, H_3, 4.85 - 5.2; H_4, 4.45; H_5, 5.93; $H_{6,6'}$, 6.8 - 7.0; methoxyl, 6.55; p-tolylsulfonyl, 2.2, 2.65, 7.55; acetyl, 7.90, 8.12.

Anal. Calcd. for $C_{18}H_{23}O_9IS$: C, 39.86; H, 4.27%; M.W., 542. Found: C, 39.89; H, 4.32%; M.W., 517.

Compound XXXIX (1.0 g) was dissolved in methanol (200 ml) containing triethylamine (10 ml) and water (100 ml) was added to the solution. After standing for sixty hours at room temperature the solution was concentrated in vacuo, the residue was dissolved in chloroform, and the chloroform solution was extracted with water (20 ml). Concentration in vacuo of the chloroform solution gave a syrup which crystallised from methanol-water to give methyl 6-deoxy-6-iodo-3-O-p-tolylsulfonyl-α-D-galactopyranoside, XL, (400 mg); m.p. 120 - 122°, $[\alpha]_D^{25}$ +141.5° (c, 1.0 in methanol).

Anal. Calcd. for $C_{14}H_{19}O_7IS$: C, 36.68; H, 4.18%; M.W., 458. Found: C, 36.76; H, 4.06%; M.W., 435.

The p.m.r. spectrum of methyl 6-deoxy-6-iodo-3-O-p-tolylsulfonyl-α-D-galactopyranoside in deuteriochloroform (Fig. 48) showed the following chemical shifts (τ value): H_1, 5.25; H_2, 6.04; H_3, 5.43; H_4, 5.74; H_5, 6.1; $H_{6,6'}$, 6.71; methoxyl, 6.57; p-tolylsulfonyl, 2.18, 2.70, 7.58. Coupling constants (c.p.s.) were: $J_{1,2}$, 3.75*; $J_{2,3}$, 9.75*; $J_{3,4}$, 3.0*; $J_{4,5}$, 1.25*; $J_{5,6}$, 7*.

To a solution of compound XL (90 mg, 0.2 mmole) in aqueous methanol (50% v/v, 30 ml) sodium periodate (250 mg, 1.2 mmole) was added and the solution was allowed to stand in the dark for forty hours at room temperature before concentrating it in vacuo. The residue was dissolved in chloroform (50 ml), extracted with water (20 ml), filtered and concentrated to give a syrup (76 mg) which crystallised on standing. The p.m.r. spectrum of the product was identical to the p.m.r. spectrum of XL showing that no reaction had occurred; therefore compound XL contains no vicinal hydroxyl groups.

(c) Methyl 6-deoxy-6-iodo-2-O-p-tolylsulfonyl-α-D-galactopyranoside (XLII).- Concentration of the mother liquors obtained after crystallisation of methyl 2,4-di-O-acetyl-6-deoxy-6-iodo-3-O-p-tolylsulfonyl-α-D-galactopyranoside from the acetylated water-insoluble fraction gave a dark brown, syrupy mixture (35 g) which was partially separated on a

silicic acid (200 g) column eluted with chloroform. A broad peak was obtained when the optical rotation of the fractions were measured. Concentration of the fractions gave a syrup (18 g, yield 11%) which, when examined by t.l.c. on a silica gel G plate developed using a 3% solution of acetone in chloroform, gave mainly one compound with R_f value 0.54. A portion of this syrup (950 mg) was further purified by chromatography using a column of silicic acid (70 g) eluted with chloroform, to give on concentration a colourless syrup (860 mg), $[\alpha]_D^{25}$ +100° (c, 2.0 in chloroform), which was shown to be methyl 3,4-di-O-acetyl-6-deoxy-6-iodo-2-O-p-tolylsulfonyl-α-D-galactopyranoside, XLI. The p.m.r. spectrum of the syrup (XLI) in deuteriochloroform is shown in Fig. 49.

Compound XLI (1.370 g, 2.5 mmole) was dissolved in methanol (50 ml) containing triethylamine (2.5 ml) and water (50 ml) was added to the solution which was allowed to stand for forty-eight hours at room temperature. Concentration *in vacuo* gave a syrup which was dissolved in chloroform (50 ml), extracted with water (10 ml), dried over anhydrous sodium sulfate, filtered and concentrated to give a syrup (1.058 g); $[\alpha]_D^{25}$ +62.1° (c, 2.3 in chloroform). Examination of this syrup by t.l.c. on a silica gel G plate developed using a 3% (v/v) solution of acetone in chloroform showed mainly one compound with R_f value 0.12 together with a weak spot with R_f value 0.46. The p.m.r. spectrum of the syrup measured in

deuteriodimethyl sulfoxide showed two methoxyl peaks. The syrup (275 mg, 0.6 mmole) was dissolved in methanol (25 ml) containing triethylamine (1 ml) and 5% palladium on charcoal (10 mg) was added. After hydrogenation for thirty minutes no further hydrogen (10 ml, 0.37 mmole) was taken up. The mixture was filtered, concentrated _in vacuo_, extracted from water (10 ml) with chloroform (2 x 25 ml), and the chloroform solution was concentrated _in vacuo_ to give a syrup (225 mg), which was acetylated by dissolving it in a mixture of acetic anhydride (5 ml) and pyridine (5 ml). Working up in the usual manner gave a light yellow syrup (243 mg) which, when examined by t.l.c. on a silica gel G plate developed using a 3% (v/v) solution of acetone in chloroform, showed two compounds with R_f values 0.28 and 0.41. When the syrup was dissolved in ethanol (2.5 ml) and allowed to stand overnight crystals formed, which were filtered to give a solid (XLIII) (60 mg), R_f value 0.41. Concentration of the filtrate gave a syrup XLIV (182 mg), $[\alpha]_D^{25}$ +95° (_c_, 1.55 in chloroform), which failed to crystallise, although shown by t.l.c. as above to consist entirely of one compound, R_f value 0.28. The p.m.r. spectrum of XLIV in deuteriochloroform (Fig. 50) showed the following chemical shifts (τ value): H_1, H_2, H_3, H_4, 4.6 - 5.4; H_5, 5.93; H_6, 8.88; methoxyl, 6.69; p-tolylsulfonyl, 2.27, 2.72, 7.56; acetyl, 7.9, 8.25. On the basis of the p.m.r. spectrum the structure of XLIV was considered to be methyl 3,4-di-_O_-

acetyl-6-deoxy-2-O-p-tolylsulfonyl-α-D-galactopyranoside. Examination of the p.m.r. spectrum of XLIII in deuteriochloroform (Fig. 51) showed it to contain one methoxyl, one p-tolylsulfonyl and one acetyl group, together with seven other protons. Since the I.R. spectrum of XLIII showed no hydroxyl absorption in the region 3100 cm^{-1} to 4000 cm^{-1}, its structure was considered to be methyl 4-O-acetyl-3,6-anhydro-2-O-p-tolylsulfonyl-α-D-galactopyranoside.

A portion (305 mg) of the syrup, obtained above by deacetylating methyl 3,4-di-O-acetyl-6-deoxy-6-iodo-2-O-p-tolylsulfonyl-α-D-galactopyranoside, was dissolved in methanol and added to an aqueous solution of 0.1 N sodium hydroxide (10 ml, 1.0 mmole). The reaction was followed by observation of the change in optical rotation of the solution which ceased after eighteen hr at room temperature, at which time the solution was neutralised to pH 7.0 by the addition of 1% acetic acid. The neutralised solution was concentrated _in vacuo_ the residue was dissolved in chloroform (50 ml), and the solution was extracted with water (25 ml), dried over anhydrous sodium sulfate and concentrated to give a syrup (251 mg), which failed to crystallise. In an attempt to obtain a crystalline derivative, the syrup (251 mg) was acetylated by dissolving it in pyridine (5 ml) and adding acetic anhydride (5 ml). After sixteen hours at room temperature the solution was concentrated _in vacuo_ at 50°, ethanol (10 ml) was added and the solution was boiled for

several minutes. On cooling, needlelike crystals (160 mg) were obtained. Recrystallisation from ethanol gave XLIII, m.p. 163 - 164°, $[\alpha]_D^{25}$ +49.3° (c, 1.0 in chloroform), which was shown to be identical to the product isolated during the hydrogenation described above.

Anal. Calcd. for $C_{16}H_{20}O_8S$: C, 51.61; H, 5.41%; M.W., 372. Found: C, 51.77; H, 5.41%; M.W., 349.

Compound XLIII (136 mg) was deacetylated by dissolving it in methanol (20 ml) containing triethylamine (1 ml) and adding water (5 ml). Forty-eight hours at room temperature gave complete deacetylation. The solution was concentrated in vacuo to a syrup which crystallised from n-propanol to give methyl 3,6-anhydro-2-O-p-tolylsulfonyl-α-D-galactopyranoside (81 mg); $[\alpha]_D^{25}$ +51° (c, 0.8 in chloroform), m.p. 139 - 140°. Jary (31) obtained the constants, $[\alpha]_D^{20}$ +54° (c, 2.2 in chloroform), m.p. 140 - 142°, for the same compound.

III. PHOTOLYSIS

1. Method and Apparatus

The light source used in all experiments was an unfiltered, medium pressure, Hanovia 250 W lamp, Serial No. 54A36. The lamp (effective length 114 mm) was immersed in the well of a quartz cooling jacket, external diameter 60 mm, through which tap water was circulated. The quartz cooling jacket was immersed in a cylindrical pyrex container, internal

diameter 70 mm, fitted with a ground glass joint at the top to support the quartz cooling jacket. A stopcock at the base of the apparatus (Fig. 1) enabled nitrogen to be bubbled through the solution to remove oxygen and to stir the solution. Solutions were added to the apparatus by means of a side arm. The volume of the apparatus, when filled to the top of the 114 mm lamp, was 220 ml of which 205 ml was directly exposed to the lamp. All photolysis experiments were done with oxygen excluded from the apparatus. Over a period of time a deposit built up in the cooling jacket of the apparatus. This deposit was removed by rinsing the cooling jacket with dilute hydrochloric acid.

2. Photolysis of Methyl α-D-Glucopyranoside

Methyl α-D-glucopyranoside (5.929 g, 30.6 mmole) and sodium bicarbonate (4.368 g, 52 mmole) were dissolved in water and the volume was adjusted to 250 ml.Part of this solution (220 ml) was photolysed for eight hr to give a colourless solution. The change in the observed rotation α_D, measured in a 1 dm tube, was from +3.75 to +3.65°. For each mole of methyl α-D-glucopyranoside present in the solution originally, titration showed that after eight hr photolysis, 0.016 mole of acid had been produced. The p.m.r. spectrum in deuterium oxide of the product after photolysis for eight hr was identical to the p.m.r. spectrum of methyl α-D-glucopyranoside.

3. Photolysis of Methyl 6-Deoxy-6-iodo-α-D-glucopyranoside

(a) In aqueous solution.- Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (8.069 g, 26.6 mmole) was dissolved in water and the volume was adjusted to 220 ml. Aliquots (10 ml) were removed from the photolysed solution at the intervals shown in Table I. A portion of each aliquot (5 ml) was titrated to pH 7.0 with sodium hydroxide (0.02 N) by the use of a pH meter. This neutral solution was then titrated for iodide with silver nitrate solution (0.02 M) using a 1% solution of dichlorofluorescein in 70% ethanol (0.5 ml) as the indicator. The end point of the titration was the change in colour of the solution from yellow to pink. Also, the optical rotation, α_D, of each aliquot was measured. The results are shown in Table I.

TABLE I

Composition of Samples Removed from the Photolysed Unbuffered Solution of Methyl 6-deoxy-6-iodo-α-D-glucopyranoside

Time (hours)	Observed rotation, α_D	Iodide liberated (mmole)	Compound I reacted (%)	Acid liberated (mmole)
0	3.787°	--	--	0
2	2.733	9.38	35.2	10.03
4	2.009	15.59	58.6	18.08
6	1.532	19.50	73.3	24.00
8	1.236	22.52	84.7	28.25
10	1.085	23.85	89.7	30.89

After 6 hours photolysis the solution turned a light yellow colour and after 10 hours photolysis the colour was dark yellow. The solution gave a positive test for iodine with starch solution. When the solution (final pH 1.1) was titrated with sodium hydroxide the solution became colourless at pH 4 - 5, but became yellow at pH 8 - 9. This alkaline solution gave a negative test for iodine with starch.

(b) In aqueous solution buffered with sodium bicarbonate

Experiment 1. Rate of photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I) in a solution buffered with sodium bicarbonate.

Compound I (9.283 g, 30.53 mmole) and sodium bicarbonate (4.363 g, 51.9 mmole) were dissolved in water and the volume was adjusted to 250 ml. Aliquots (10 ml), removed from the photolysed solution at intervals, were analysed for: (i) iodide ion, (ii) sodium bicarbonate by adding a portion (2 ml) of each aliquot to hydrochloric acid (0.02 N, 25 ml) and after just bringing the solution to boiling to remove carbon dioxide, the solution was cooled and back-titrated with sodium hydroxide using phenolphthalein as the indicator, (iii) optical rotation, α_D. The results of these experiments are given in Table II. It can be seen that after ten hours photolysis, of the 26.86 mmole of I present originally, 26.20 mmole of iodide ion had been liberated, also of the original 44.25 mmole of sodium bicarbonate present, 29.85 mmole was neutralised after photolysis for ten hours.

TABLE II

Composition of Samples Removed from the Solution of Methyl 6-deoxy-6-iodo-α-D-glucopyranoside Photolysed in the Presence of Sodium Bicarbonate

Time (hr)	Observed rotation, α_D	Iodide liberated (mmole)	Compound I reacted (%)	Acid liberated (mmole)
0	3.792	--	--	0
2	2.705	11.4	42.4	10.49
4	2.134	19.02	70.8	19.17
6	1.853	23.12	86.1	24.31
8	1.699	25.26	94.0	27.62
10	1.622	26.20	97.5	29.85
10*	1.615	26.36		30.15

* The ten hour photolysis sample was allowed to stand at room temperature in a closed flask for twelve hours before being analysed.

During photolysis the solution turned a light yellow colour which darkened on standing. It was found that the solution gave a negative test for iodine with starch and that the yellow colour disappeared on acidification.

Experiment 2. Separation of photolysis products by Celite column chromatography

(i) Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (8.042 g, 26.4 mmole) was dissolved in an aqueous solution containing sodium bicarbonate (3.888 g, 46.3 mmole) and the volume was made up to 220 ml. After being photolysed for ten hr the solution was light yellow in colour, but gave no reaction when tested for iodine with starch solution. The solution was concentrated *in vacuo*, prior to chromatography on a Celite column, and the p.m.r. spectrum of the crude product (Fig. 4) was measured in deuterium oxide.

The first fraction eluted from the column (0.3 litre) gave on concentration *in vacuo* a syrup (1.024 g) which crystallised on standing, and showed the same p.m.r. spectrum and R_f value (solvent systems A and B) as methyl 6-deoxy-6-iodo-α-D-glucopyranoside.

Concentration *in vacuo* of the second fraction (0.4 litre) gave a light yellow syrup (1.168 g) which crystallised on standing. Examination of the fractions by paper chromatography, using solvent system A, indicated only one compound, R_f value 0.67, but with some streaking of the chromatogram. It was possible to eliminate this streaking by passing an aqueous solution of the compound successively through columns of Amberlite IR 120 resin (H^+, 5 ml) and Amberlite IRA 400 resin (OH^-, 5 ml) to give on concentrating *in vacuo* a colourless syrup, methyl 6-deoxy-α-D-glucopyranoside (III)

(950 mg, yield 23%), which rapidly crystallised. Examination by paper chromatography as before revealed only one compound, R_f value 0.67 without streaking. Paper chromatography in solvent system B showed one compound, R_f value 0.73. Recrystallisation from ethyl acetate gave material with $[\alpha]_D^{25}$ +151° (c, 2.3 in water), and m.p. 97 - 98°. From the literature (32) the physical constants for methyl 6-deoxy-α-D-glucopyranoside (III) are: $[\alpha]_D$ +148° (in water), m.p. 98 - 99°. A mixture of methyl 6-deoxy-α-D-glucopyranoside with the compound recovered from the photolysis product showed no melting point depression. The p.m.r. spectrum of methyl 6-deoxy-α-D-glucopyranoside in deuteriopyridine (Fig. 5) showed the following chemical shifts (τ value): H_1, 5.08; H_2, 6.05; H_3, 5.70; H_4, 6.46; H_5, 6.00; H_6, 8.52; methoxyl, 6.68. Coupling constants (c.p.s.) were: $J_{1,2}$, 3.5*; $J_{2,3}$, 9.5; $J_{3,4}$, 8.5; $J_{4,5}$, 9.5; $J_{5,6}$, 6.0. Methyl 6-deoxy-α-D-glucopyranoside (580 mg) was acetylated in the usual way with acetic anhydride (10 ml) and pyridine (10 ml) to give a syrup (1.012 g) which was crystallised from n-propanol to give methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside, IV, (405 mg) m.p. 55 - 58°. The melting point was unchanged after a further three recrystallisations from Skellysolve B; $[\alpha]_D^{25}$ +152° (c, 1.15 in chloroform). Helferich (33) reports m.p. 75°, $[\alpha]_D^{25}$ +159.2°, for IV. The p.m.r. spectrum of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside in deuteriochloroform (Fig. 6) showed the

following chemical shifts (τ value): H_1, H_2, H_4, 4.95 - 5.35; H_3, 4.53; H_5, 6.05; H_6, 8.77; methoxyl, 6.57; acetyl, 7.92, 7.94, 7.98.

Concentration in vacuo of the third fraction eluted from the column gave a syrup (4.0 g) which when examined by paper chromatography, solvent system A, showed a compound with R_f value 0.20 which gave an immediate white coloured spot with the silver nitrate spray reagent. The compound gave a yellow precipitate on testing for iodide with silver nitrate. When a sample of sodium iodide was chromatographed on paper in the above manner it showed exactly the same characteristics.

Concentration in vacuo of the fourth fraction (1.2 litre) gave a brown syrup (553 mg) which could not be crystallised. The syrup was purified by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 10 ml) and Amberlite IRA 400 resin (OH^-, 10 ml). Concentration in vacuo of the eluate gave a colourless syrup, V, (237 mg, 5.8%) which rapidly crystallised. Paper chromatography of V (solvent system A) showed one compound with R_f value 0.13, without the extensive streaking present before treatment with the ion-exchange resin. Recrystallisation from methanol gave a compound, with $[\alpha]_D^{25}$ +174.4° (c, 1.0 in water), m.p. 243 - 245°, whose structure was shown to be methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside, V.

Anal. Calcd. for $C_{14}H_{26}O_{10}$: C, 47.45; H, 7.40%,

M.W., 354. Found: C, 47.44; H, 7.36%; M.W., 338.

An attempt was made to examine the dark syrup eluted finally from the Celite column with water (3.30 g). An aqueous solution of a portion of this material (1.75 g) was passed through a column containing Amberlite IRA 400 resin (OH^-, 60 ml) and the column was then eluted with a further 250 ml of water. To remove organic acids from this column it was washed with 2% sodium acetate (500 ml) and the resulting sodium acetate washings passed through a column of Amberlite IR 120 resin (H^+, 110 ml) to remove sodium ions. Concentration _in vacuo_ of the eluate gave a syrup, X, (298 mg) whose I.R. spectrum showed strong absorption at 1730 cm^{-1}.

(ii) Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (8.106 g, 26.67 mmole) and sodium bicarbonate (3.825 g, 45.54 mmole) were dissolved in water and the volume of the solution made up to 220 ml. The solution was photolysed for ten hr, concentrated _in vacuo_, and the residue was separated on a Celite column as described previously. Concentration _in vacuo_ of appropriate fractions gave methyl 6-deoxy-6-iodo-α-D-glucopyranoside (1.235 g, 4.06 mmole), methyl 6-deoxy-α-D-glucopyranoside, III, (1.129 g, crude yield 28%) and dimer, V, (184 mg, yield 4.6%). Elution of the Celite column with water yielded, after concentration _in vacuo_, a dark syrup (2.941 g) which was passed as an aqueous solution through a column of Amberlite IR 120 resin (H^+, 25 ml). Concentration _in vacuo_ of the eluate gave a syrup (1.226 g). This material did not

contain an iodine atom and hence represents ∿30% yield of the amount of methyl 6-deoxy-6-iodo-α-D-glucopyranoside consumed in the reaction.

(iii) Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (1.908 g, 6.276 mmole) and sodium bicarbonate (1.429 g, 17.0 mmole) were dissolved in water and the volume adjusted to 220 ml. The solution, after photolysis for four hr, gave a negative test for formaldehyde with chromotropic acid. Concentration *in vacuo* of the photolysed solution gave a brown syrup which was separated on a Celite column (100 g). Collection and concentration *in vacuo* of appropriate fractions followed by deionisation by ion-exchange resins as before gave the following compounds: methyl 6-deoxy-α-D-glucopyranoside (171 mg), yield 15.3%; dimer, V, (116 mg), yield 10.4%.

Experiment 3. Separation of photolysis products by silicic acid chromatography.

An aqueous solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside (8.106 g, 26.67 mmole) with sodium bicarbonate (3.900 g, 46.42 mmole), total volume 220 ml, was photolysed for ten hours. The photolysed solution was concentrated *in vacuo* and the last traces of water were removed by freeze-drying. The residue was dissolved in pyridine (100 ml) and acetic anhydride (50 ml) was added. After standing overnight at room temperature the mixture was concentrated *in vacuo* to a syrup which was dissolved in ethanol (50 ml) and allowed to stand for two hr before being concentrated *in vacuo*. The syrup was

chromatographed on a silicic acid column (Mallinchrodt 100 Mesh, 200 g). An initial elution with chloroform removed several compounds without effecting a complete separation. The first of these compounds was methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside (I), identified by its p.m.r. spectrum, followed by methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside (IV) also identified by its p.m.r. spectrum. The material from the last portion (2.514 g) of the chloroform eluate was further separated by rechromatographing it on a silicic acid column (80 g) using chloroform to elute the column. Two well-separated fractions were obtained, the first fraction (633 mg) was shown to be methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside, while the second fraction (1.207 g) could not be crystallised and was deacetylated by dissolving it in methanol (100 ml) containing triethylamine (10 ml) and water (20 ml). After standing for sixteen hours the solution was concentrated in vacuo and the residue was deionised by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 20 ml) and Amberlite IRA 400 resin (OH^-, 20 ml). Concentration in vacuo of the eluate from the columns gave a colourless syrup (198 mg) which crystallised and was shown to be the dimer, V.

A second major peak was eluted from the original silicic acid column with 1% (v/v) ethanol-chloroform.

Concentration in vacuo yielded a light yellow syrup, XI, (1.323 g) whose molecular weight was determined to be 800 (osmometric). Since this fraction was shown to contain no iodine this represents a yield of approximately 20% based on unrecovered starting material. A portion of XI (173 mg) was deacetylated using the method of Zemplen (34) by dissolving it in dry methanol (10 ml) and adding 3 ml of a solution prepared by dissolving sodium (0.5 g) in dry methanol (100 ml). After standing at room temperature for sixteen hr the solution was concentrated in vacuo and the sodium ions removed by shaking an aqueous solution of the product with Amberlite IR 120 resin (H^+, 2 ml). Concentration in vacuo gave a syrup, XII, whose p.m.r. spectrum is shown in Fig. 12 and whose I.R. spectrum showed the absorption at 1630 cm^{-1} with a stronger absorption at 1710 cm^{-1} possibly due to a carboxylic acid group. An attempt to reduce XII using sodium borohydride caused no change in the I.R. spectrum. Examination of XII by t.l.c. on a silica gel G plate (solvent A) gave only streaking without discrete spots; however, with ethanol, acetic acid, water (5:4:1, by vol.) one spot, R_f value 0.68, was obtained. Compound XII (55 mg) dissolved in water (10 ml) was heated with Amberlite IR 120 resin (H^+, 1 ml) for twenty-four hr on a steam bath. When examined by t.l.c. no change was observed in the chromatographic pattern.

Experiment 4. Separation of photolysis products by carbon column chromatography.

Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (8.101 g, 26.65 mmole) with sodium bicarbonate (3.745 g, 44.6 mmole) was dissolved in water and the volume adjusted to 220 ml. Nitrogen was bubbled through the solution while it was photolysed for ten hr. The final optical rotation of the solution, measured in a 1 dm tube was $+2.155^{\circ}$. Concentration *in vacuo* of the solution gave a brown syrup which was separated by carbon column chromatography using the conditions described on p. 10. Six main peaks, A, B, C, D, E, and F were eluted from the column.

Fraction A Concentration *in vacuo* of this fraction gave a dark syrup (130 mg, yield 3.7%) which when examined by p.m.r. and t.l.c. appeared to consist largely of methyl α-D-glucopyranoside.

Fraction B Concentration *in vacuo* of the fractions making up this broad peak gave a syrup (873 mg) which, when examined by t.l.c. on a silica gel G plate developed with solvent system A, showed only one compound with R_f value 0.53 which was identified as methyl 6-deoxy-α-D-glucopyranoside. The yield was 27%.

Fraction C Concentration *in vacuo* of this fraction gave a brown syrup (309 mg) which when examined by t.l.c. on a silica gel G plate with solvent system A showed three compounds with R_f values 0.25, 0.50, 0.62 of which the slowest moving compound appeared to be the major component. The mixture was

chromatographed on a microcrystalline cellulose column using solvent system A to elute the column. Investigation of the fractions (15 ml) eluted from the column by measuring their optical rotation revealed one major peak together with several minor peaks which were not investigated further. Concentration in vacuo of the major peak gave a syrup, XIII, (114 mg), $[\alpha]_D^{25}$ +49.6° (c, 1.6 in methanol), which when examined by t.l.c. on a microcrystalline cellulose plate (solvent system A) revealed one spot with R_f value 0.35. The p.m.r. spectrum of XIII in deuterium oxide is shown in Fig. 13 and the spectrum in deuteriopyridine is shown in Fig. 14. Decoupling experiments (with deuteriopyridine as the solvent) revealed protons with the following chemical shifts (τ value): H_1, 5.09; H_2, 6.21; H_3, 5.58; $H_{1'}$, 4.08; $H_{2'}$, 5.9; $H_{3'}$, 5.36; methoxyl 6.69. Coupling constants (c.p.s.) were: $J_{1,2}$, 3.5; $J_{2,3}$, 9.0; $J_{3,4}$, 8.0; $J_{1',2'}$, 7.5; $J_{2',3'}$, 9.0; $J_{3',4'}$, 9.0. The I.R. spectrum of XIII (KBr disc) showed an absorption at 1730 cm^{-1} with a weaker absorption at 1640 cm^{-1}. The molecular weight of the syrup XIII was found to be 282 (osmometric).

Fraction D Concentration in vacuo of the fractions making up this peak gave a syrup (492 mg) which when examined by t.l.c. on a silica gel G plate in solvent system A showed two compounds with R_f values 0.57 and 0.68, the major compound being the slower moving compound. Crystallisation from n-propanol gave fine light brown crystals, XIV, (51 mg), m.p. 184 - 187°,

$[\alpha]_D^{25}$ +97.8° (c, 1.4 in water), which when examined by t.l.c. as above showed one compound, R_f value 0.57. The I.R. spectrum of XIV (KBr disc) is shown in Fig. 15 and the p.m.r. spectrum in deuteriopyridine is shown in Fig. 16.

Fraction E Concentration *in vacuo* of these fractions gave a syrup (492 mg) which when examined by t.l.c. as above gave some streaking mainly centred at R_f value 0.35, the same R_f value as the dimer V. The syrup was passed through a column of microcrystalline cellulose (300 x 35 mm). Concentration *in vacuo* of the major fraction gave a syrup (202 mg) which was dissolved in water and passed through a column of Amberlite IR 120 resin (H^+, 5 ml) on top of Amberlite IRA 400 resin (OH^-, 5 ml). Concentration *in vacuo* of the eluate gave a colourless syrup (162 mg, yield 5%) which crystallised and was shown to be the dimer, V.

Fraction F Concentration *in vacuo* of this large peak gave a syrup (2.57 g, recovered 31.7%) which readily crystallised and was shown to be methyl 6-deoxy-6-iodo-α-D-glucopyranoside.

Experiment 5. Analysis of products formed by the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I) by gas-liquid chromatography of the *O*-trimethylsilyl ethers.

Compound I (9.279 g, 30.5 mmole) and sodium bicarbonate (4.337 g, 51.6 mmole) were dissolved in water and the volume adjusted to 250 ml. A portion of this solution (225 ml) was added to the photolysis apparatus and samples (~6 ml) were removed from the solution while it was photolysed at the intervals shown in Table III. From each sample an

accurately measured aliquot (5 ml) was pipetted into a flask containing a solution of pentaerythritol (5 ml, 0.16 mmole) and 1.0 N sodium hydroxide (5 ml). The solutions were allowed to stand for 22 hr before being passed through a column of Amberlite MB1 resin (10 ml) and eluted with water (150 ml). Each eluate was concentrated in vacuo, dissolved in pyridine (2 ml) and reacted with hexamethyldisilazane (1 ml) and trimethylchlorosilane (0.5 ml) at room temperature for 15 min. The reaction mixture was concentrated in vacuo and the residue was extracted with methylene chloride. Gas-liquid chromatography of each sample gave the results shown in Table III. The values shown were calculated by comparing the peak areas with the results obtained when the O-trimethylsilyl ethers of a mixture containing known quantities of methyl α-D-glucopyranoside, methyl 6-deoxy-α-D-glucopyranoside, and dimer V, was chromatographed.

TABLE III

Percentage Yields of Methyl α-D-glucopyranoside, Methyl 6-deoxy-α-D-glucopyranoside (III), and Dimer (V), Determined by Gas-Liquid Chromatography of the O-Trimethylsilyl Ethers.

Time (min)	40	80	160	320	600
Methyl α-D-glucopyranoside	-	0.2%	0.4%	1.0%	1.7%
Methyl 6-deoxy-α-D-glucopyranoside (III)	2.6%	4.1%	7.8%	13.3%	19.3%
Dimer (V)	-	-	0.2%	2.3%	3.6%

Experiment 6. Photolysis of Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I) in deuterium oxide.

A mixture of I (2.575 g, 8.47 mmole) with sodium bicarbonate (1.217 g, 14.5 mmole) was exchanged three times with deuterium oxide. After exchanging, the mixture was dissolved in deuterium oxide (70 ml) in the same photolysis apparatus as was used previously. During the photolysis time of sixteen hr nitrogen was bubbled through the solution three times for several minutes to stir the solution. The solvent was removed by freeze-drying and when the p.m.r. spectrum of this solvent was examined it showed a sharp singlet at 6.63τ which was attributed to methanol. A known amount of acetone (0.02 ml) was added to 10 ml of this liquid and the p.m.r. spectrum taken. Comparison of the relative integrations of the methanol and acetone singlets showed that approximately three mmole of methanol was present in the photolysed solution. The residue, after freeze-drying, was dissolved in water (15 ml) and separated on a carbon-Celite column (45 x 330 mm). The fractions obtained were as follows: Fraction B, 250 mg; Fraction C, 98 mg; Fraction D, 76 mg; Fraction E, 152 mg; Fraction F, 240 mg. Each fraction was shown by silica gel G t.l.c. (solvent system A) to be similar to the fraction with the same letter isolated in Experiment 4.

Fraction B was recrystallised from ethyl acetate to give crystals (28 mg) whose I.R. spectrum could not be distinguished from that of authentic methyl 6-deoxy-α-D-

glucopyranoside. A portion of the mother liquor (72 mg) was acetylated by dissolving it in a mixture of pyridine (2 ml) and acetic anhydride (2 ml) and allowing the solution to stand overnight at room temperature before concentrating in vacuo. Water (15 ml) was added to the residue to destroy any acetic anhydride remaining and the mixture extracted with chloroform (15 ml). The chloroform solution was worked up in the usual manner to give a colourless syrup (93 mg) which crystallised from Skellysolve B to give a compound (15 mg), m.p. 57 - 58°, whose mass spectrum was indistinguishable from the mass spectrum of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside.

Experiment 7. Photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d (XV).

Compound XV (1.908 g, 6.276 mmole) with sodium bicarbonate (1.428 g, 17.0 mmole) was dissolved in water and the volume made up to 220 ml. Nitrogen was bubbled through the solution while it was photolysed for four hr. The change in optical rotation of the solution during the photolysis reaction was from +0.861 to +0.340°. Concentration in vacuo of the photolysed solution gave a syrup which was separated by the use of n-butanol-water partition chromatography on Celite (100 g) to give three compounds.

(i) Methyl 6-deoxy-α-D-glucopyranoside-1-d. Concentration in vacuo of the fractions containing the first compound eluted from the Celite column gave a syrup (326 mg)

which was purified by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 5 ml) and Amberlite IRA 400 resin (OH^-, 5 ml) to give, after concentration *in vacuo*, a colourless syrup (175 mg, 15.6% yield). Examination by t.l.c. on a silica gel G plate revealed a single compound with the same R_f value as methyl 6-deoxy-α-D-glucopyranoside. The syrup was acetylated with pyridine and acetic anhydride to give a colourless syrup (275 mg) which crystallised from n-propanol to give methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-1-d, XVII, (50 mg); m.p. 53 - 56°. The p.m.r. spectrum of methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-1-d (Fig. 18) in deuteriochloroform showed the following chemical shifts (τ value): H_2, 5.09; H_3, 4.62; H_4, 5.25; H_5, 6.16; H_6, 8.82; methoxyl, 6.67; acetyl, 8.00, 8.04, 8.07. Coupling constants (c.p.s.) were: $J_{2,3}$, 10; $J_{3,4}$, 9.5; $J_{4,5}$, 9.5; $J_{5,6}$, 6.0. Comparison of the integration of the C-methyl doublet at 8.82τ with the integration of the methoxyl singlet at 6.67τ suggested that there was no appreciable amount of deuterium at carbon-6.

A comparison of the mass spectrum of methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-1-d (XVII) (Fig. 20) with the mass spectrum of methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside (IV) (Fig. 21) confirmed the fragmentation pattern shown in Fig. 17 (p. 104). The m/e value for the fragments 171, 153, 111, postulated to contain H_1, increased to 172, 154, and 112 respectively, while the

fragments with m/e 184 and 142 were unchanged as would be expected since they were not considered to include H_1. The most accurate method of measuring the percentage of deuterium at carbon-6 was to compare the relative intensities of the m/e 142 and m/e 143 peaks obtained from the mass spectra of IV and XVII. The result was for IV, 142 : 143 :: 1.0 : 0.210 and for XVII, 142 : 143 :: 1.0 : 0.227. These results suggest that deuterium has replaced hydrogen at carbon-6 to the extent of 1.5% in the case of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside-1-d (XVII).

(ii) Methyl α-D-glucopyranoside-1-d. Concentration *in vacuo* of the second fraction gave a brown syrup which was deionised by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 15 ml) and Amberlite IRA 400 resin (OH^-, 15 ml) to give, on concentration *in vacuo*, a syrup (33 mg), which was shown by p.m.r. and t.l.c. on a silica gel G plate, developed in solvent system A, to be methyl α-D-glucopyranoside-1-d (yield 2.7%).

(iii) Methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside-1-d]-6-yl)-α-D-glucopyranoside-1-d (XVI). The final fraction was concentrated *in vacuo*. Deionisation of the resulting syrup by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 6 ml) and Amberlite IRA 400 resin (OH^-, 6 ml) gave, after concentration *in vacuo* a colourless syrup, XVI, (104 mg, yield 9.3%) which rapidly crystallised on standing. From the p.m.r. spectrum of XVI in deuterium oxide it was apparent

that compound XVI was the 1-deuterio analogue of the "glucose dimer" V. Compound XVI was acetylated with acetic anhydride and pyridine to give on crystallisation from ethanol, methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-gluco-pyranoside-1-d]-6-yl)-α-D-glucopyranoside-1-d hexa-acetate, XVIII, (130 mg); $[\alpha]_D^{25}$ +165° (c, 2.0 in chloroform), m.p. 184 - 185°. The p.m.r. spectrum of XVIII in deuteriochloroform (Fig. 19) showed the following chemical shifts (τ value): H_2, 5.17; H_3, 4.58; H_4, 5.15; H_5, 6.1 - 6.35; $H_{6,6'}$, 8.25 - 8.4; methoxyl, 6.61; acetyl, 7.92, 7.96, 7.99. Coupling constants (c.p.s.) were: $J_{2,3}$, 10; $J_{3,4}$, 9.5; $J_{4,5}$, 9.5.

Experiment 8. Photolysis of methyl 6-deoxy-6-iodo-α-D-gluco-pyranoside in the presence of methyl α-D-glucopyranoside. Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (4.0 g, 13.16 mmole), sodium bicarbonate (1.755 g, 20.84 mmole) and methyl α-D-glucopyranoside (5.101 g, 26.81 mmole) were dissolved in water and the volume was adjusted to 220 ml. After photolysing for eight hr the solution was acidified to pH 3.0 by the addition of 0.1 N hydrochloric acid and then concentrated *in vacuo* at 40°. The residue was dissolved in water and separated on a carbon-Celite column (400 x 55 mm).

Measurement of the optical rotation of the fractions obtained enabled the following three peaks to be separated. The first peak eluted from the column gave on concentration *in vacuo* a syrup (5.660 g) which was recrystallised from methanol to give methyl α-D-glucopyranoside (3.093 g)

together with a black intractible mother liquor which appeared to be mainly methyl α-D-glucopyranoside. Concentration *in vacuo* of the second peak left a syrup (554 mg) which was purified by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 5 ml) and Amberlite IRA 400 resin (OH^-, 5 ml) to give, on concentration *in vacuo* of the eluate, a clear syrup (510 mg, yield 22%) which crystallised and was shown to be methyl 6-deoxy-α-D-glucopyranoside. Concentration *in vacuo* of the third peak left a syrup (289 mg) which, when purified with ion-exchange resins as described above, yielded a syrup (161 mg, yield 7%) which crystallised and was shown to be the dimer V.

4. Proof of Structure of Methyl 6-Deoxy-6-*C*-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside (V).

The p.m.r. spectrum of the dimer V, in deuteriopyridine (Fig. 7) was very similar to the p.m.r. spectrum of the 6-deoxy compound III, when only the ring protons were considered; the chemical shifts obtained were (τ value): H_1, 4.98; H_2, 5.98; H_3, 5.61; H_4, 6.27; H_5, ∿5.95; $H_{6,6'}$, 7.25 - 8.0; methoxyl, 6.62. The multiplet at 7.25 - 8.0τ integrated for four protons when the methoxyl signal at 6.62τ was assumed to represent six protons. Coupling constants (c.p.s.) were: $J_{1,2}$, 3.5*; $J_{2,3}$, 9.5; $J_{3,4}$, 8.5*; $J_{4,5}$, 9.5.

Compound V (37.7 mg, 0.1065 mmole) was dissolved in sodium acetate buffer solution (pH 3.8, 23 ml) in a 50 ml volumetric flask. Sodium periodate solution (25 ml, 0.8 mmole),

prepared by dissolving sodium periodate (3.424 g, 16 mmole) in sodium acetate buffer solution and adjusting the volume to 500 ml, was added to the volumetric flask and the volume was made up to 50 ml with sodium acetate buffer solution. At the same time a blank solution was prepared omitting only compound V. Both solutions were shaken well and kept in the dark at room temperature. Aliquots (5 ml) were removed from both solutions at intervals (Table IV) and added to a mixture of saturated sodium bicarbonate (10 ml) and 20% potassium iodide (w/v) (2 ml). After fifteen minutes in the dark, the solutions were titrated to determine the liberated iodine by the method of Mueller and Friedberger (36) using standard 0.005 M sodium arsenite (37). Just before the yellow colour of iodine disappeared a 1% solution of starch (0.5 ml) was added. The results are recorded in Table IV and a plot of moles of periodate consumed against time of reaction is given in Fig. 8.

TABLE IV

Oxidation of Methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside (V) with Sodium Periodate.

Time (min)	5	40	90	150	300	420	630	1500	1800
Na_2AsO_2 (ml)	1.83	4.89	5.71	6.21	7.01	7.30	7.73	8.82	9.25
Moles $NaIO_4$ consumed for each mole of V	0.86	2.30	2.68	2.92	3.29	3.43	3.63	4.14	4.34

It is evident from these results that four moles of sodium periodate are consumed by each mole of dimer, V, present.

The dimer, V, (98 mg, 0.323 mmole) was dissolved in sodium acetate buffer solution (20 ml, pH 3.8) and sodium periodate (406 mg, 1.9 mmole) was added. The solution was allowed to stand in the dark at room temperature for sixteen hours, sodium borohydride (253 mg, 6.8 mmole) was added and the solution was allowed to stand for a further eight hours. Amberlite IR 120 resin (H^+, 15 ml) was added and the mixture heated on a steam bath for sixteen hours, cooled, filtered and concentrated <u>in vacuo</u>. To remove boric acid, methanol (10 ml) was added and the solution was boiled for several minutes before concentrating <u>in vacuo</u>. This procedure was repeated three times to give a syrup which was deionised by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 5 ml) and Amberlite IRA 400 resin (OH^-, 5 ml). Concentrating <u>in vacuo</u> gave a clear syrup (46 mg) whose p.m.r. spectrum in deuterium oxide showed two peaks, a multiplet in the region 6.2 - 6.5τ and a multiplet in the region 8.25 - 8.5τ integrating in the ratio 3:2. These results are compatible with a 3,4-dideoxy-L-<u>threo</u>-hexitol structure for this fragment. The compound was acetylated with acetic anhydride and pyridine in the usual manner to give a colourless syrup, VI, (72 mg) $[\alpha]_D^{25}$ +3° (chloroform), which when examined by t.l.c. on a silica gel G plate using a 3%

(v/v) solution of acetone in chloroform revealed one spot, R_f 0.37, with streaking. Gas-liquid chromatography of VI using a column temperature of 200° gave a single peak, retention time 11.5 min. The p.m.r. spectrum of VI (Fig. 9) was consistant with the structure 3,4-dideoxy-tetra-O-acetyl-L-*threo*-hexitol.

Compound VI (50 mg, 0.16 mmole) was dissolved in methanol (5 ml) and 0.2 N sodium hydroxide (10 ml, 2.0 mmole) was added to the solution which was allowed to stand at room temperature for twenty-four hours before it was concentrated *in vacuo* to a syrup. This syrup was dissolved in water (10 ml), acidified with 25% acetic acid, and then oxidized by the addition of sodium periodate (200 mg, 0.93 mmole); the reaction mixture being allowed to stand in the dark at room temperature for sixteen hours. Sodium borohydride (300 mg, 7.9 mmole) was added to the solution, which still contained sodium borohydride when tested after seven hours. The solution was shaken with Amberlite IR 120 resin (H^+, 10 ml) for fifteen minutes, before the solution was filtered and the filtrate concentrated *in vacuo*. Boric acid was removed by adding methanol (20 ml) and boiling for several minutes before concentrating *in vacuo*; the procedure being repeated three times. The remaining syrup was deionised by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 10 ml) and Amberlite IRA 400 resin (OH^-, 10 ml). Concentration *in vacuo*

of the eluate gave a syrup, VII, whose p.m.r. spectrum in deuterium oxide was identical to the p.m.r. spectrum of 1,4-butanediol. Compound VII was acetylated in the usual manner to give a colourless syrup VIII, whose p.m.r. spectrum (Fig. 10) was identical to the p.m.r. spectrum of 1,4-butane diacetate. Gas-liquid chromatography of VIII using a column temperature of 100° gave a single peak with a retention time of sixteen min; the same result was obtained for an authentic sample of 1,4-butanediol diacetate.

Compound V was acetylated in the usual manner with acetic anhydride to give, after crystallisation from ethanol, colourless needles of methyl 6-deoxy-6-_C_-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside hexa-acetate, IX; $[\alpha]_D^{25}$ +161.6° (_c_, 1.4 in chloroform), m.p. 183 - 186°.

Anal. Calcd. for $C_{26}H_{38}O_{16}$: C, 51.48; H, 6.31%; M.W., 606. Found: C, 51.65; H, 5.98%; M.W., 611.

The p.m.r. spectrum of IX in deuteriochloroform (Fig. 11) showed protons with the following chemical shifts (τ value): H_1, H_2, H_4, 5.05 - 5.3; H_3, 4.59; H_5, 6.1 - 6.4; $H_{6,6'}$, 8.3 - 8.4; methoxyl, 6.63; acetyl, 7.95, 7.99, 8.02.

5. Photolysis of Methyl 6-Deoxy-6-iodo-α-D-glucopyranoside in the Presence of Acetaldehyde.

Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (8.107 g, 26.67 mmole), sodium bicarbonate (7.780 g, 92.62 mmole) and acetaldehyde (75 ml, 1.33 mole) were dissolved in water and

the volume was adjusted to 220 ml. Nitrogen was bubbled through the solution for a few minutes to remove oxygen before the solution was photolysed for ten hours. At the end of this time the solution was still basic and the volume of the solution was 220 ml. The photolysed solution was concentrated in vacuo to a syrup whose p.m.r. spectrum showed the major product from the photolysis to be methyl 6-deoxy-α-D-glucopyranoside (III). The products were separated on a Celite column (200 g). The first fraction eluted from the column gave on concentration in vacuo a dark syrup (3.391 g) from which unchanged methyl 6-deoxy-6-iodo-α-D-glucopyranoside (1.843 g) was crystallised. Examination of the next fraction revealed a partial separation of two compounds which were more completely separated by rechromatographing the fractions containing both compounds on another Celite (40 g) column. The fastest moving of these two compounds was obtained as a syrup (2.890 g, 79% yield) which crystallised from ethyl acetate to yield methyl 6-deoxy-α-D-glucopyranoside (III) (1.464 g). Concentration in vacuo of fractions containing the slower moving compound gave a syrup (methyl 6,8-dideoxy-D(and L)-glycero-α-D-gluco-octopyranoside, XXV) (300 mg) which when examined by t.l.c. on a silica gel G plate (solvent system A) showed a single compound with R_f value 0.54. The p.m.r. spectrum of XXV was measured in deuterium oxide (Fig. 27). Irradiating at 6.05 caused the collapse of the doublet at 8.76τ to a singlet and partially decoupled the

multiplet in the region 8.0 - 8.3τ. In an attempt to spread the chemical shifts of the ring protons the p.m.r. spectrum of XXV (100 Mc.p.s.) was measured in deuteriopyridine; however, due possibly to the presence of two epimers, a triplet at 5.0τ, two methoxyls at 6.65τ and 6.61τ, and two barely separated doublets at 8.6τ were observed, instead of the expected anomeric doublet at ∿5.0τ, single methoxyl at ∿6.6τ, and doublet at ∿8.6τ.

Compound XXV (114 mg, 0.51 mmole) was dissolved in water (15 ml) and heated on a steam bath with Amberlite IR 120 resin (H^+, 1 ml) for twenty hours to hydrolyse the methyl glycoside. After cooling and filtering off the resin, sodium periodate (700 mg, 3.27 mmole) was added and the solution was allowed to stand at room temperature for twelve hours before adding sodium borohydride (300 mg, 7.93 mmole). Excess sodium borohydride was destroyed after twelve hours by shaking the solution with Amberlite IR 120 resin (H^+, 10 ml) before filtering and concentrating the filtrate _in vacuo_. Boric acid was removed from the residue by treatment with methanol as described previously and the remaining syrup was deionised by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 5 ml) and Amberlite IRA 400 resin (OH^-, 5 ml). Concentration _in vacuo_ gave a syrup (XXVI) (25 mg) whose p.m.r. spectrum was identical to the p.m.r. spectrum of 1,3-butanediol.

6. Photolysis of Methyl 6-Deoxy-6-iodo-α-D-glucopyranoside in the Presence of Methyl 6-Deoxy-α-D-*xylo*-hex-5-enopyranoside (XIX)

Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (1.911 g, 6.28 mmole), methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside (2.40 g, 13.63 mmole), and sodium bicarbonate (1.432 g, 17.0 mmole) were dissolved in water and the volume adjusted to 220 ml. The solution was photolysed for 4 hr, concentrated *in vacuo*, and the residue was separated on a Celite column (150 g) to give the following fractions:

Fraction A The first fraction was shown to contain methyl 6-deoxy-α-D-glucopyranoside (∿250 mg, yield ∿15%) and unchanged methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside (∿1.260 g). These quantities were calculated from the p.m.r. spectrum of the mixture.

Fraction B Concentration *in vacuo* of the second fraction gave a syrup which was deionised by passing an aqueous solution of the syrup through a column of Amberlite MB1 resin (25 ml). The eluate was concentrated *in vacuo* to a syrup (53 mg) which was shown by paper chromatography (solvent systems A and B) to be mainly methyl α-D-glucopyranoside.

Fraction C Concentration *in vacuo* of the third fraction gave a syrup which was deionised with ion-exchange resin, as above, to give a syrup (100 mg) which crystallised and was shown by paper chromatography (solvent systems A and B) to be the dimer, V.

Fraction D After the above fractions were eluted, the Celite column was eluted with water to give, on concentration *in vacuo*, a syrup. An aqueous solution of the syrup was passed through a column of Amberlite IR 120 resin (H^+, 30 ml). Concentration *in vacuo* of the eluate gave a syrup (926 mg) whose p.m.r. spectrum was similar to the p.m.r. spectrum of the polymeric material (X) obtained in previous experiments by elution of the Celite column with water.

7. Photolysis of Methyl 6-Deoxy-6-iodo-α-D-glucopyranoside in the Presence of Allyl Alcohol.

Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (2.000 g, 6.58 mmole), sodium bicarbonate (1.060 g, 12.62 mmole) and redistilled allyl alcohol (20 g, 345 mmole) were dissolved in water and the volume of the solution was adjusted to 220 ml. The optical rotation of the solution, measured in a decimeter tube, changed from +0.933 to +0.568° when the solution was irradiated for four hr. Concentration *in vacuo* of the photolysed solution gave a syrup (5.0 g) which was deionised by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 25 ml) and Amberlite IRA 400 resin (OH^-, 25 ml). Concentration *in vacuo* of the eluate gave a syrup (2.0 g) whose p.m.r. spectrum (Fig. 23) measured in deuterium oxide showed broad peaks in the regions 6.0 - 6.5τ and 7.5 - 9.2τ, together with a singlet at 6.55τ which was assigned to a methoxyl group. A doublet at 8.67τ with a

spacing of 6.5 c.p.s. indicated the presence of a small amount of methyl 6-deoxy-α-D-glucopyranoside. The syrup was chromatographed on a Sephadex G25 (medium, 100 g) column eluted with water, to give a broad peak when the optical rotation of each fraction (10 ml) was measured. This broad peak was split into seven fractions and each fraction was filtered and concentrated _in vacuo_. When the specific rotation of each of the fractions was measured the following results were obtained: $[\alpha]_D^{25}$ +25, +42, +52, +54, +49, +49, +38°. Measurement of the molecular weight of each fraction gave the following results: 716, 392, 359, 293, 280, 252, 284.

8. Photolysis of Methyl 6-Deoxy-6-iodo-α-D-glucopyranoside in the Presence of Formaldehyde.

(a) Rate of photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside in the presence of formaldehyde.- Compound I (8.122 g, 26.72 mmole), sodium bicarbonate (3.827 g, 45.56 mmole) and formaldehyde solution (23 ml, ∿299 mmole) were dissolved in water and the volume adjusted to 230 ml. Nitrogen was passed through the solution while it was photolysed for ten hr, and aliquots (10 ml) were removed at the intervals (hr): 0, 1, 2, 3, 4.17, 5, 6, 8, 10. The optical rotation of each aliquot was measured. A solution (25 ml) of 0.02 N hydrochloric acid was added to 2 ml of each aliquot; the resulting solution was boiled, cooled, and back titrated with 0.02 N sodium hydroxide using phenolphthalein as the indicator. The results obtained are shown in Table V.

TABLE V

Composition of Samples Removed from the Solution of Methyl 6-deoxy-6-iodo-α-D-glucopyranoside Photolysed in the Presence of Formaldehyde

Time (hr)	Observed rotation, degrees	Sodium bicarbonate in solution (mmole)	Acid liberated in reaction (mmole)
0	3.65	45.81	0
1	--	38.67	7.14
2	2.72	32.25	13.56
3	--	26.90	18.91
4.17	2.01	21.05	24.76
5	1.83	18.41	27.40
6	1.66	16.31	29.50
8	1.44	11.85	33.96
10	1.34	11.16	34.65

Examination of the product after ten hr photolysis by t.l.c. on a silica gel G plate (solvent system A) revealed a new compound with R_f value 0.46.

(b) Isolation of products from the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside in the presence of formaldehyde.-

(i) Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (8.02 g, 26.4 mmole), sodium bicarbonate (3.9 g, 46.4 mmole),

and formaldehyde solution (22 ml, ∿286 mmole) were dissolved in water and the volume was adjusted to 220 ml. The solution, stirred by bubbling nitrogen through it, was photolysed for eight and a half hr before being concentrated _in vacuo_. Excess formaldehyde was removed by repeatedly adding water and concentrating _in vacuo_ until the weight was constant. Separation of the residue was achieved by chromatography on a Celite (200 g) column to give the following fractions:

Fraction A Concentration _in vacuo_ of the first fraction eluted from the Celite column gave a syrup (1.164 g) which rapidly crystallised and was shown to be unchanged methyl 6-deoxy-6-iodo-α-D-glucopyranoside, recovery 14.5%.

Fraction B Concentration _in vacuo_ of the second fraction eluted from the Celite column gave a syrup (1.024 g) which crystallised on standing and was shown to be methyl 6-deoxy-α-D-glucopyranoside, yield 25.5%.

Fraction C Concentration _in vacuo_ of the third fraction gave a syrup (1.484 g) containing sodium iodide. In order to remove the sodium iodide and other impurities the syrup was acetylated by adding to it a mixture of pyridine (20 ml) and acetic anhydride (10 ml), the mixture being worked up in the usual manner to give a syrup (1.238 g). This syrup was purified by chromatography on a column of silicic acid (30 g) using chloroform as the eluent. One major fraction was obtained which on concentration gave a syrup, XXII, (574 mg, yield 6.8%) which crystallised from ethanol-water; m.p. 61-61.5°,

$[\alpha]_D^{25}$ +142° (c, 1.0 in chloroform). Proof that the compound was methyl 2,3,4,7-tetra-O-acetyl-6-deoxy-α-D-gluco-heptopyranoside (XXII) is given below (c).

Anal. Calcd. for $C_{16}H_{24}O_{10}$: C, 51.06; H, 6.43%; M.W., 376. Found: C, 51.11; H, 6.19%; M.W., 380.

The remaining fractions were divided into four groups, concentrated in vacuo and acetylated with pyridine and acetic anhydride. Each acetylated fraction was left overnight and then concentrated in vacuo, the residue was dissolved in chloroform and the chloroform solution was extracted with water. The dried chloroform solution was in each case concentrated and the residue fractionated on a silicic acid column. The only compound identified was methyl 2,3,4,6-tetra-O-acetyl-α-D-glucopyranoside (106 mg, yield 1.3%).

(ii) The photolysis reaction was repeated using methyl 6-deoxy-6-iodo-α-D-glucopyranoside (8.107 g, 26.7 mmole), sodium bicarbonate (3.857 g, 45.7 mmole), and formaldehyde solution (46 ml, ∿598 mmole). Separation on a Celite column as before gave the following fractions:

Fraction A On concentrating in vacuo, this fraction gave a syrup (779 mg, recovery 9.6%) which crystallised and was shown to be methyl 6-deoxy-6-iodo-α-D-glucopyranoside.

Fraction B Concentration in vacuo of this fraction gave a syrup (1.452 g, yield 33.8%), which failed to crystallise, but was shown by paper chromatography and by examination of

its p.m.r. spectrum to be methyl 6-deoxy-α-D-glucopyranoside.

Fraction C Concentration in vacuo of this fraction gave a syrup which was purified by passing an aqueous solution successively through columns of Amberlite IR 120 resin (H^+, 50 ml) and Amberlite IRA 400 resin (OH^-, 50 ml), to remove sodium iodide and other impurities. Concentration in vacuo of the eluate gave a colourless syrup, methyl 6-deoxy-α-D-gluco-heptopyranoside, XXI, (510 mg, yield 10%), $[\alpha]_D^{25}$ +149° (c, 1.52 in methanol), which failed to crystallise. Compound XXI on acetylation in pyridine and acetic anhydride was shown to give methyl 2,3,4,7-tetra-O-acetyl-6-deoxy-α-D-gluco-heptopyranoside.

Fraction D Concentration in vacuo followed by deionising as before gave a syrup (178 mg) which was shown by examination of its p.m.r. spectrum and by t.l.c. to be methyl α-D-gluco-pyranoside.

(iii) The photolysis reaction was repeated using methyl 6-deoxy-6-iodo-α-D-glucopyranoside (8.133 g, 26.75 mmole), sodium bicarbonate (3.906 g, 46.5 mmole), and formaldehyde solution (184 ml, ~2.6 mole). Separation on a Celite column as before gave the following fractions:

Fraction A A syrup (919 mg, 11.3% recovery) was obtained which crystallised and was shown to be methyl 6-deoxy-6-iodo-α-D-glucopyranoside.

Fraction B A syrup (1.771 g, yield 42%) was obtained which failed to crystallise, but was shown by its p.m.r. spectrum

and by paper chromatography to be methyl 6-deoxy-α-D-gluco-pyranoside.

Fraction C This fraction was deionised as described previously and concentrated *in vacuo* to give a syrup (574 mg, yield 11.6%), which was shown to be methyl 6-deoxy-α-D-*gluco*-heptopyranoside.

(c) Proof of structure of methyl 6-deoxy-α-D-*gluco*-heptopyranoside (XXI).- The p.m.r. spectrum of XXII (Fig. 24) in deuteriochloroform showed the following chemical shifts (τ value): H_1, H_2, H_4, 5.0 - 5.25; H_3, 4.56; H_5, 6.12; $H_{6,6'}$, 8.0 - 8.25; $H_{7,7'}$, 5.8; methoxyl, 6.66; four acetyl, 7.9 - 8.04. On the basis of this data XXII was tentatively assigned the structure methyl 2,3,4,7-tetra-*O*-acetyl-6-deoxy-α-D-*gluco*-heptopyranoside.

The p.m.r. spectrum of methyl 6-deoxy-α-D-*gluco*-heptopyranoside in deuteriopyridine (Fig. 25) showed the following chemical shifts (τ value): H_1, 4.96; H_2, 5.96; H_3, 5.58; H_4, 6.23; H_5, $H_{7,7'}$, 5.6 - 6.0; H_6, 7.25; $H_{6'}$, 7.9; methoxyl, 6.59. Coupling constants (c.p.s.) were: $J_{1,2}$*, 3.5; $J_{2,3}$, 9.0; $J_{3,4}$*, 9.0; $J_{4,5}$, 9.0.

Methyl 6-deoxy-α-D-*gluco*-heptopyranoside (46.1 mg, 0.222 mmole) was dissolved in buffer solution (pH 3.8), sodium periodate solution (25 ml, 0.8 mmole) was added and the volume was adjusted to 50 ml by the addition of buffer solution. At the same time a blank solution was prepared without methyl 6-deoxy-α-D-*gluco*-heptopyranoside and aliquots (5 ml) were removed from both solutions at the intervals shown

in Table VI. These aliquots were added to a solution, prepared by mixing saturated sodium bicarbonate (10 ml) and 20% potassium iodide (2 ml), which was allowed to stand in the dark at room temperature for fifteen minutes before the liberated iodine was titrated with sodium arsenite. The results (Table VI) show that two moles of periodate are consumed for each mole of methyl 6-deoxy-α-D-<u>gluco</u>-heptopyranoside, which is in agreement with the postulated structure.

TABLE VI

Oxidation of Methyl 6-deoxy-α-D-<u>gluco</u>-heptopyranoside (XXI) with Sodium Periodate.

Time (min)	6	95	150	270	480	720	1440
moles periodate consumed per mole of XXI	0.49	1.72	1.97	2.03	1.99	2.07	2.23

Methyl 6-deoxy-α-D-<u>gluco</u>-heptopyranoside (150 mg, 0.72 mmole) was dissolved in water (20 ml) and sodium periodate (600 mg, 2.804 mmole) was added. The solution was allowed to stand in the dark at room temperature for twelve hours before being reduced by the addition of sodium borohydride (1.0 g, 26.2 mmole). After six hours, excess sodium borohydride was destroyed by shaking the solution with Amberlite IR 120 resin (H^+, 25 ml) and the solution was then heated for two hours on

a steam bath to hydrolyse the acetal linkage. Concentration *in vacuo* gave a syrup XXIII which was found by paper chromatography to have R_f values identical to those of 1,2,4-butanetriol (solvent system A and B). The p.m.r. spectrum of XXIII in deuterium oxide was identical to the spectrum of authentic 1,2,4-butanetriol and showed two multiplets at 6.0 - 6.6τ and 8.1 - 8.6τ which gave integrated intensities in the ratio of 5:2.

Compound XXIII was acetylated by adding a solution of acetic anhydride (2 ml) in pyridine (2 ml) and allowing the mixture to stand at room temperature for twenty-four hr before it was concentrated *in vacuo*. Excess acetic anhydride was removed from the residue by concentration *in vacuo* with ethanol to give a syrup XXIV (45 mg), $[\alpha]_D^{25}$ +9.0° (*c*, 2.2 in methanol), whose p.m.r. spectrum (Fig. 26) was identical to the p.m.r. spectrum of 1,2,4-butanetriol triacetate. The I.R. spectra, in chloroform, of the two compounds were identical, and on examination by gas-liquid chromatography both compounds showed a retention time of 21.7 min when the column temperature was programmed from 100 - 200° at 2.9°/ min.

9. Photolysis of Methyl 6-Deoxy-6-iodo-α-D-glucopyranoside in the Presence of Methyl 6-Deoxy-α-D-*xylo*-hex-5-enopyranoside (XIX) and Acetaldehyde.

Methyl 6-deoxy-6-iodo-α-D-glucopyranoside (4.00 g, 13.2 mmole), methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside (2.325 g, 13.2 mmole), acetaldehyde (58 g, 1.32 mole), and

sodium bicarbonate (5.175 g, 61.6 mmole) were dissolved in water and the volume of the solution was adjusted to 220 ml. The solution was photolysed for eight hr, concentrated _in vacuo_ and the residue separated on a Celite column to give the following fractions:

Fraction A The first material eluted from the Celite column (1.5 g) could not be identified, but appeared to consist mainly of products formed by the polymerisation of acetaldehyde.

Fraction B The second fraction was a mixture of methyl 6-deoxy-α-D-glucopyranoside (~1.5 g), methyl 6-deoxy-α-D-_xylo_-hex-5-enopyranoside (~1.2 g), and methyl 6,8-dideoxy-α-D-_gluco_-octopyranosid-7-ulose, XLV, (~500 mg). The relative quantities of each compound were estimated from the p.m.r. spectrum of the mixture. To a portion of the mixture (297 mg), dissolved in water (10 ml), sodium borohydride (200 mg) was added and the solution was allowed to stand for four hr before the excess sodium borohydride was destroyed by adding acetic acid. The solution was passed through a column of Amberlite IR 120 resin (H^+, 15 ml) and the eluate was concentrated _in vacuo_. Examination of the trimethylsilyl derivative of the residue by g.l.c. revealed in addition to a peak with the same retention time as the trimethylsilyl derivative of methyl 6-deoxy-α-D-glucopyranoside, a peak with the same retention time as the trimethylsilyl derivative of methyl 6,8-dideoxy-D(and L)-_glycero_-α-D-_gluco_-octopyranoside. This peak was not found when the trimethylsilyl derivative of the mixture before reduction

was examined by g.l.c.

Portion of Fraction B (1.0 g) was acetylated in the usual way with acetic anhydride in pyridine and the residue was separated by chromatography on a column of silicic acid (60 g) eluted with chloroform. Concentration _in vacuo_ of appropriate fractions gave a syrup (245 mg) which crystallised from n-propanol to give methyl 2,3,4-tri-_O_-acetyl-6,8-dideoxy-α-D-_gluco_-octopyranosid-7-ulose, XLVI, (115 mg); m.p. 118 - 120°, $[\alpha]_D^{25}$ +144° (_c_, 0.8 in chloroform).

Anal. Calcd. for $C_{15}H_{22}O_9$: C, 52.02; H, 6.40%. Found: C, 52.09; H, 6.52%.

The p.m.r. spectrum of XLVI in deuteriochloroform showed protons with the following chemical shifts (τ value): H_1, H_2, H_4, 5.04 - 5.26; H_3, 4.52; H_5, 5.52 - 5.76; $H_{6,6'}$, 7.1 - 7.64; $H_{8,8,8'}$ 7.79; methoxyl, 6.53; acetyl, 7.90, 7.94, 7.97. Decoupling experiments showed that the signals assigned to H_3, H_4, H_5, $H_{6,6'}$ were coupled together in the expected manner. The I.R. spectrum of XLVI showed a shoulder (1720 cm^{-1}) on the acetyl peak (1750 cm^{-1}).

Fraction C By examination of the p.m.r. spectrum of the third fraction, together with g.l.c. investigation of the trimethylsilyl derivative, it was apparent that the main component was methyl 6,8-dideoxy-α-D-_gluco_-octopyranosid-7-ulose, XLV, (∿500 mg) with smaller amounts of methyl 6-deoxy-α-D-glucopyranoside (∿175 mg) and methyl 6,8-dideoxy-D(and L)-_glycero_-α-D-_gluco_-octopyranoside (∿225 mg).

Fraction D The fourth fraction was deionised by passing an aqueous solution through a column of Amberlite MB1 resin (35 ml). The eluate was concentrated *in vacuo* to a colourless syrup (96 mg) which on examination by paper chromatography (solvent systems A and B) appeared to contain mainly the dimer, V, (∿65 mg) together with a smaller amount of methyl α-D-glucopyranoside (∿30 mg). These quantities were estimated from the p.m.r. spectrum of the syrup.

Fraction E Concentration *in vacuo* of the solution obtained by eluting the Celite column with water gave a syrup which was passed in an aqueous solution through a column of Amberlite IR 120 resin (H^+, 25 ml). The eluate was concentrated *in vacuo* to a syrup (80 mg) whose p.m.r. spectrum was similar to the spectrum of the polymer, X.

10. Photolysis of Methyl 6-Deoxy-6-iodo-α-D-galactopyranoside

(a) Isolation of products from the photolysis of methyl 6-deoxy-6-iodo-α-D-galactopyranoside (XXVII).- Compound XXVII (4.00 g, 13.15 mmole) and sodium bicarbonate (1.825 g, 21.73 mmole) were dissolved in water and the volume was adjusted to 225 ml. When the solution was photolysed for seven and one half hr the observed optical rotation of the solution, α_D, changed from +2.511 to +1.276°. Aliquots (5 ml) were removed from the solution both before and after it was photolysed and were analysed immediately for sodium bicarbonate. For each mole of methyl 6-deoxy-6-iodo-α-D-galactopyranoside present initially in the solution, 1.08 moles of sodium bicarbonate were neutralised during photolysis of the solution. To each

sample a further quantity of sodium hydroxide (0.964 mmole) was added and the solutions, after standing for one hr, were titrated with hydrochloric acid to pH 7 using a pH meter. For each mole of XXVII present initially in the solution, 0.31 mole of sodium hydroxide was consumed. It was apparent that reaction of methyl 6-deoxy-6-iodo-α-D-galactopyranoside with sodium hydroxide to give either methyl α-D-galacto-pyranoside or methyl 3,6-anhydro-α-D-galactopyranoside must be quite slow under these conditions, since there was very little consumption of sodium hydroxide in the initial aliquot. The remainder of the photolysis solution (213.5 ml) was freeze-dried until the volume was reduced to ∿20 ml. Examination of the p.m.r. spectrum of the distillate showed a singlet at 6.6τ which was considered to be due to methanol.

This photolysis procedure was repeated using compound XXVII (4.000 g, 13.16 mmole), sodium bicarbonate (1.749 g, 20.82 mmole) with a total volume of 225 ml. The change in the observed optical rotation during the seven and a half hr photolysis time was from +2.536 to +1.200°. In this case the initial and final aliquots were not titrated to determine the amount of sodium bicarbonate consumed until four days after the solution was photolysed. It was found that for each mole of methyl 6-deoxy-6-iodo-α-D-galactopyranoside present initially in the solution, 1.42 moles of sodium bicarbonate was neutralised during the reaction compared to the 1.58 moles of sodium bicarbonate available. It should be noted that

titration of the initial aliquot showed that the calculated amount of sodium bicarbonate was present even though the sample had been left for four days.

The remainder of the solution (211.5 ml) was freeze-dried, combined with the previous photolysis product, titrated with 2.0 N sulfuric acid to pH 5.5 and concentrated *in vacuo* at 40°. The syrup was separated using a charcoal-Celite column into the following fractions:

Fraction A Concentration of the collected fractions *in vacuo* gave a syrup (560 mg) which rapidly darkened on standing. Examination by t.l.c. using a silica gel G plate (solvent system A) showed a single compound, R_f value 0.40, with extensive streaking. Chromatography on a microcrystalline cellulose column (150 g) using solvent system A as eluent yielded a fraction (119 mg) which gave a p.m.r. spectrum identical to that of authentic methyl α-D-galactopyranoside, yield 2.6%.

Fraction B Concentration *in vacuo* of the fractions from this broad peak gave a syrup (942 mg) which crystallised on standing. On examination by t.l.c. on a silica gel G plate (solvent system A) it was found to consist of a single compound with R_f value 0.50. Recrystallisation from ethyl acetate gave methyl 6-deoxy-α-D-galactopyranoside (XXVIII) (410 mg); $[\alpha]_D^{25}$ +198.5° (*c*, 1.0 in water), m.p. 156 - 157°. MacPhillamy and Elderfield (38) obtained the constants, $[\alpha]_D^{25}$ +190.0° (*c*, 4.1 in water), m.p. 155 - 156°, for methyl 6-deoxy-α-D-galactopyranoside. The p.m.r. spectrum of methyl 6-deoxy-α-D-galactopyranoside is shown in

Fig. 33. The p.m.r. spectrum of the initial product (942 mg) was indistinguishable from the p.m.r. spectrum of recrystallised methyl 6-deoxy-α-D-galactopyranoside. Calculating on the basis of the amount of starting material consumed in the reaction the yield of methyl 6-deoxy-α-D-galactopyranoside was 23.1%.

Anal. Calcd. for $C_7H_{14}O_5$: C, 47.18; H, 7.92%. Found: C, 47.13, H, 7.65%.

Methyl 6-deoxy-α-D-galactopyranoside (XXVIII) (170 mg) was dissolved in a mixture of pyridine (10 ml) and acetic anhydride (5 ml). After standing for twenty-four hours at room temperature the solution was worked up in the usual manner to give a syrup (299 mg). Crystallisation of the syrup from ethanol-water gave methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-galactopyranoside (146 mg); $[\alpha]_D^{25}$ +151.5° (c, 3.0 in chloroform), m.p. 59 - 64° (39). The p.m.r. spectrum of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-galactopyranoside is shown in Fig. 34.

Fraction C Concentration in vacuo of appropriate fractions gave a syrup (252 mg) which crystallised on standing. When the syrup was examined by t.l.c. on a silica gel G plate (solvent system A) two well defined spots were obtained with R_f value 0.53 (XXIX) and 0.46 (XXX) as well as a streaked spot, R_f value approximately 0.08. Chromatography on a microcrystalline cellulose column (40 x 500 mm) using solvent system A as eluent gave two partially resolved peaks with considerable streaking. Concentration in vacuo of the fractions representing the first peak eluted from the column gave XXIX (52 mg), $[\alpha]_D^{25}$ +177.4°

(*c*, 1.9 in methanol), which was shown by t.l.c. to be one compound with R_f value 0.53. The p.m.r. spectrum of XXIX in deuterium oxide is shown in Fig. 35 and the I.R. spectrum of XXIX (KBr disc) is shown in Fig. 36. Concentration *in vacuo* of the fractions constituting the second peak gave a syrup, XXX (83 mg), $[\alpha]_D^{25}$ +140.3° (*c*, 1.6 in methanol), which was shown by t.l.c. to consist mainly of one compound R_f value 0.46, but with a small amount of streaking.

Fraction D Concentration *in vacuo* of this fraction gave a colourless syrup (392 mg) which darkened on standing. The I.R. spectrum (film) of the syrup showed a weak absorption at 1645 cm^{-1} and a strong absorption at 1725 cm^{-1}. Examination of the syrup by t.l.c. on a silica gel G plate (solvent system A) showed four compounds with R_f values 0.05, 0.37, 0.46, 0.53. Although a partial separation was achieved on a cellulose column eluted with solvent system A it was not found possible to achieve a complete separation of any one compound. The p.m.r. spectra of partially resolved mixtures showed absorption in the region 7.9 - 8.5τ indicative of methylene protons.

Fraction E Concentration *in vacuo* of the fractions making up this sharp peak gave a syrup (406 mg) which crystallised on standing. Recrystallisation was achieved by dissolving the crystals in a small quantity of water and diluting with methanol, on standing the dimer, methyl 6-deoxy-6-*C*-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-galactopyranoside (XXXI), crystallised (253 mg); $[\alpha]_D^{25}$ +189° (*c*, 1.0 in water), m.p.

271 - 272°, yield 6.5%. The p.m.r. spectrum of XXXI in deuterium oxide is shown in Fig. 37.

Anal. Calcd. for $C_{14}H_{26}O_{10}$: C, 47.45; H, 7.4%. Found: C, 46.92; H, 7.14%.

Fraction F Concentration *in vacuo* of the fractions constituting this peak gave a colourless syrup (887 mg) which immediately crystallised. Examination by t.l.c. on a silica gel G plate (solvent system A) revealed one compound with R_f value 0.66 together with a small amount of streaking. Recrystallisation from methanol gave colourless crystals (584 mg) of methyl 6-deoxy-6-iodo-α-D-galactopyranoside; $[\alpha]_D^{25}$ +146.2° (*c*, 1.0 in water), m.p. 173 - 174°.

Anal. Calcd. for $C_7H_{13}O_5I$: C, 27.64; H, 4.38%. Found: C, 27.59; H, 4.10%.

(b) Proof of Structure of methyl 6-deoxy-6-*C*-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-galactopyranoside (XXXI).- Compound XXXI (92 mg) was acetylated by adding it to a mixture of pyridine (10 ml), acetic anhydride (5 ml) and heating the mixture on a steam bath for three hr. Concentration *in vacuo*, followed by boiling with ethanol to remove acetic anhydride and elution with chloroform through a silicic acid column gave a syrup (160 mg) which crystallised from ethanol to give methyl 6-deoxy-6-*C*-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-galactopyranoside hexa-acetate (XXXII) (104 mg); $[\alpha]_D^{25}$ +161° (*c*, 1.4 in chloroform), m.p. 175 - 176°.

Anal. Calcd. for $C_{26}H_{38}O_{16}$: C, 51.48; H, 6.31%; M.W., 606. Found: C, 51.37; H, 6.02%; M.W., 611.

The p.m.r. spectrum of XXXII in deuteriochloroform (Fig. 38) showed protons with the following chemical shifts (τ value): H_1, 5.06; H_2, 4.88; H_3, H_4, 4.58 - 4.76; H_5, 6.08; $H_{6,6'}$, 8.1 - 8.7; methoxyl, 6.62; acetyl, 7.84, 7.92, 8.02.

Compound XXXI (60 mg, 0.17 mmole) was dissolved in water (10 ml) containing sodium periodate (225 mg, 1.05 mmole) and the solution was allowed to stand in the dark at room temperature for eighteen hours before sodium borohydride (500 mg, 13.16 mmole) was added. After twenty hours at room temperature the excess sodium borohydride was destroyed by the addition of Amberlite IR 120 resin (H^+, 20 ml); hydrolysis of the acetal group was accomplished by heating the mixture on a steam bath for twenty hours. The mixture was filtered to remove the resin, the filtrate was concentrated *in vacuo*, methanol (10 ml) was added and the solution was boiled for several minutes before concentrating *in vacuo* again. This procedure was repeated three times to remove boric acid. To remove any remaining ions an aqueous solution was passed successively through columns of Amberlite IR 120 resin (H^+, 10 ml) and Amberlite IRA 400 resin (OH^-, 10 ml), the column being eluted with water (150 ml) and the eluate concentrated *in vacuo* to a colourless syrup which was acetylated by dissolving it in pyridine (5 ml) and acetic anhydride (5 ml). After standing for sixteen hours the reaction mixture was poured

into ice (40 g), allowed to stand for two hr, extracted into chloroform (50 ml) and the chloroform solution worked up in the usual manner to give on concentration _in vacuo_ a syrup, XXXIII, (60 mg); $[\alpha]_D^{25}$ +0.3° (_c_, 3.0 in chloroform). Examination of the syrup by t.l.c. on a silica gel G plate developed using a 3% (v/v) solution of acetone in chloroform revealed one compound with R_f value 0.37 with a small amount of streaking. Gas-liquid chromatography of XXXIII at 200° gave only one peak with a retention time of 11.5 min. When a mixture of XXXIII with compound VI, the product obtained from degradation of the "glucose" dimer (V), was chromatographed under the same conditions only one peak, retention time 11.5 min, was obtained. The p.m.r. spectrum of XXXIII (Fig. 39) and the p.m.r. spectrum of VI (Fig. 9) were identical, as were the two I.R. spectra. On this basis the structure of XXXIII is 3,4-dideoxy-tetra-_O_-acetyl-L-_threo_-hexitol.

11. Photolysis of Methyl 6-Deoxy-6-iodo-α-D-galactopyranoside in the Presence of Formaldehyde.

(a) Isolation of products from the photolysis of methyl 6-deoxy-6-iodo-α-D-galactopyranoside (XXVII) in the presence of formaldehyde.- Compound XXVII (4.000 g, 13.16 mmole) and sodium bicarbonate (1.793 g, 21.35 mmole) were dissolved in water, formaldehyde solution (60 ml, ~760 mmole) was added and the volume was adjusted to 230 ml. An initial aliquot (5 ml) was removed and the remaining solution (225 ml) was photolysed for eight hours to give a colourless solution,

volume 221 ml, pH 8.1. Analysis of the initial and final aliquots showed that for each mole of XXVII initially present in the solution, 1.33 moles of sodium bicarbonate was consumed during the photolysis reaction.

To obtain material for separation the above photolysis procedure was repeated twice using the same quantities of XXVII, sodium bicarbonate, and formaldehyde, but no aliquots were removed from the solution. The resulting two solutions were combined together and concentrated _in vacuo_ to give the product plus paraformaldehyde which was removed by repeatedly adding water to the mixture and then concentrating _in vacuo_ until finally a constant weight was obtained. Separation of the syrup was achieved by using a charcoal-Celite column to give the following fractions:

Fraction A Concentration _in vacuo_ of the first fraction gave a dark syrup (5.521 g) which on investigation by t.l.c. on a silica gel G plate (solvent system A) gave streaking without clear spots.

Fraction B The second fraction on concentration _in vacuo_ yielded a syrup (3.36 g) which when examined by t.l.c. on a silica gel G plate (solvent system A) revealed two compounds with R_f values 0.55, 0.42. These two compounds were separated chromatographically using a microcrystalline cellulose column (200 g, 40 x 500 mm) eluted with solvent system A. The optical rotation of each of the fractions (10 ml) was measured and revealed two major peaks, as well as one other minor compound

which was not identified or investigated further. Concentration *in vacuo* of the first major peak eluted from the column gave a syrup (909 mg) which rapidly crystallised, showed only one spot with R_f value 0.55 when examined by t.l.c. as above, and was shown to be methyl 6-deoxy-α-D-galactopyranoside, yield 25.8%. Concentration *in vacuo* of the second major peak eluted from the column gave a syrup (780 mg) which failed to crystallise, although examination by t.l.c. as above showed only one spot with R_f value 0.42. This compound was shown to be methyl 6-deoxy-α-D-*galacto*-heptopyranoside XXXIV, yield 19%.

Fraction C The third fraction gave on concentration *in vacuo* a syrup (2.0 g) which crystallised immediately and when examined by t.l.c. on a silica gel G plate (solvent system A) showed only one compound with R_f value 0.66, identical to the starting material, methyl 6-deoxy-6-iodo-α-D-galactopyranoside.

(b) Proof of structure of methyl 6-deoxy-α-D-*galacto*-heptopyranoside (XXXIV).- Compound XXXIV (780 mg) was dissolved in a mixture of pyridine (15 ml) and acetic anhydride (15 ml) and the solution was allowed to stand for twenty hours before it was worked up in the usual manner to give a syrup which failed to crystallise. This syrup was further purified using a silicic acid column (70 g, 300 x 25 mm) with chloroform as the eluent. Measurement of the optical activity of fractions eluted from the column revealed one peak which on concentration *in vacuo* gave a clear syrup XXXV (686 mg); $[\alpha]_D^{25}$ +140.5° (*c*, 1.06 in chloroform). Although examination of the syrup by

t.l.c. on a silica gel G plate developed using a 3% solution of acetone in chloroform revealed only one compound with R_f value 0.38, the compound, XXXV, failed to crystallise and was analysed as a syrup.

Anal. Calcd. for $C_{16}H_{24}O_{10}$: C, 51.06; H, 6.43%; M.W., 376. Found: C, 51.45; H, 6.34%; M.W., 371.

The p.m.r. spectrum of XXXV, methyl 2,3,4,7-tetra-*O*-acetyl-6-deoxy-α-D-*galacto*-heptopyranoside, in deuteriochloroform (Fig. 40) showed the following chemical shifts (τ value): H_1, 5.05; H_2, 4.88; H_3, H_4, 4.55 - 4.72; H_5, 5.89; $H_{6,6'}$, 8.05 - 8.35; $H_{7,7'}$, 5.84; methoxyl, 6.63; acetyl, 7.85, 7.93, 7.96, 8.03.

Compound XXXV (580 mg, 1.54 mmole) was dissolved in anhydrous methanol and cooled to 0° before adding a solution of 0.5 N barium methoxide (1 ml) (42). The temperature of the solution was maintained at 0° until, after twenty-four hours, examination of the reaction mixture by t.l.c. showed deacetylation was complete. After concentration *in vacuo* the product was deionised by passing an aqueous solution through a column of Amberlite IR 120 resin (H^+, 5 ml). Concentration *in vacuo* of the eluate yielded a syrup (320 mg, 1.54 mmole) which rapidly crystallised. Recrystallisation from n-propanol gave methyl 6-deoxy-α-D-*galacto*-heptopyranoside (XXXIV) (200 mg); $[\alpha]_D^{25}$ +186° (*c*, 1.92 in water), m.p. 108 - 109°.

Anal. Calcd. for $C_8H_{16}O_6$: C, 46.15; H, 7.75%. Found: C, 46.20; H, 7.54%.

The p.m.r. spectrum of XXXIV in deuteriopyridine (Fig. 41) showed the following chemical shifts (τ value): H_1, 4.90; H_2, 5.47; H_3, H_4, H_5, 5.5 - 5.8; $H_{6,6'}$, 7.25 - 7.95; $H_{7,7}$, 5.90; methoxyl, 6.57. Coupling constants (c.p.s.) were: $J_{1,2}$, 3.5; $J_{2,3}$, 9.5; $J_{6,7}$, 6.5.

The mass spectrum of the trimethylsilyl derivative of XXXIV, prepared using the procedure of Golding _et al_ (19), was almost identical to the mass spectrum of the trimethylsilyl derivative of methyl 6-deoxy-α-D-_gluco_-heptopyranoside (XXI). Only small differences in the relative intensity of various peaks could be detected.

12. Photolysis of Methyl 6-Deoxy-6-iodo-α-D-galactopyranoside in the Presence of Methyl 6-Deoxy-α-D-_xylo_-hex-5-enopyranoside and Acetaldehyde.

Methyl 6-deoxy-6-iodo-α-D-galactopyranoside (4.00 g, 13.2 mmole), methyl 6-deoxy-α-D-_xylo_-hex-5-enopyranoside (2.391 g, 13.58 mmole), acetaldehyde (58 g, 1.32 mole), and sodium bicarbonate (6.00 g, 71.4 mmole) were dissolved in water and the volume of the solution was adjusted to 220 ml. The solution was photolysed for eight hr, concentrated _in vacuo_ and the residue was partially separated on a Celite column to give the following fractions:

Fraction A The first fraction eluted from the column appeared to be similar to the polymeric acetaldehyde material, of low optical rotation, obtained previously.

Fraction B Concentration *in vacuo* of the second fraction gave a syrup (895 mg) which appeared from its p.m.r. spectrum to be almost completely methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside.

Fraction C Concentration *in vacuo* of the third fraction gave a syrup (2.367 g) which appeared from its p.m.r. spectrum to consist of a mixture of methyl 6-deoxy-α-D-galactopyranoside and methyl 6,8-dideoxy-α-D-*gluco*-octopyranosid-7-ulose. The syrup was crystallised from ethyl acetate to give methyl 6-deoxy-α-D-galactopyranoside (900 mg) and a mother liquor, (1.34 g) estimated by p.m.r. spectroscopy to contain methyl 6-deoxy-α-D-galactopyranoside (∿340 mg) and methyl 6,8-dideoxy-α-D-*gluco*-octopyranosid-7-ulose, XLV, (∿1.0 g). Acetylation of the mother liquor with acetic anhydride (10 ml) in pyridine (10 ml) in the usual manner gave a syrup which was partially crystallised from n-propanol to yield crystalline methyl 2,3,4-tri-*O*-acetyl-6,8-dideoxy-α-D-*gluco*-octopyranosid-7-ulose, XLVI, (413 mg) which showed a p.m.r. spectrum identical to that of the same material isolated in a previous experiment.

Fraction D Concentration *in vacuo* of the fourth fraction gave a syrup (1.015 g) which appeared from its p.m.r. spectrum to contain mainly methyl 6-deoxy-α-D-galactopyranoside (∿900 mg) together with a small quantity of methyl 6,8-dideoxy-α-D-*gluco*-octopyranosid-7-ulose, XLV, (∿100 mg).

Fraction E Concentration *in vacuo* of the fifth fraction gave a syrup (210 mg) which appeared from its p.m.r. spectrum to

contain methyl 6-deoxy-α-D-galactopyranoside (~90 mg) and methyl 6,8-dideoxy-D(and L)-glycero-α-D-galacto-octopyranoside (XLVII) (~120 mg).

Fraction F Concentration in vacuo of the sixth fraction gave a syrup which was deionised by passing an aqueous solution through a column of Amberlite MB1 resin (20 ml). Concentration in vacuo of the eluate gave a colourless syrup (34 mg) which appeared from its p.m.r. spectrum to be virtually pure methyl 6,8-dideoxy-D(and L)-glycero-α-D-galacto-octopyranoside (XLVII).

The p.m.r. spectrum of XLVII in deuterium oxide (Fig. 30) showed protons with the following chemical shifts (τ value): H_1, 5.2; H_2, H_3, H_4, H_5, H_7, 5.9 - 6.2; $H_{6,6'}$, 8.0 - 8.5; $H_{8,8,8'}$, 8.78; methoxyl, 6.57. Irradiation of the multiplet at 5.9 - 6.2τ (includes H_7) caused a partial collapse of the multiplet at 8.0 - 8.5τ ($H_{6,6'}$) and caused the doublet at 8.78τ ($H_{8,8,8}$) to collapse to a singlet.

Fraction G Concentration in vacuo of the seventh fraction gave a syrup which was deionised by passing an aqueous solution through a column of Amberlite MB1 resin (25 ml). Concentration in vacuo of the eluate yielded a colourless syrup (70 mg) which was identified as methyl α-D-galactopyranoside from its p.m.r. spectrum.

Fraction H Concentration in vacuo of the eighth fraction gave a syrup which was deionised by passing an aqueous solution through a column of Amberlite MB1 resin (25 ml) to give on concentration in vacuo of the eluate, a colourless syrup (160 mg) which crystallised from methanol (118 mg) to give

a compound identified as methyl 6-deoxy-6-_C_-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-glucopyranoside (XLVIII); $[\alpha]_D^{25}$ +182° (_c_, 1.0 in water), m.p. 245 - 247°. The p.m.r. spectrum of XLVIII measured in deuteriopyridine (Fig. 31) showed protons with the following chemical shifts (τ value): H_1, 4.88 (doublet, spacing 3.25 c.p.s.); $H_{1'}$, 4.96 (doublet, spacing 3.5 c.p.s.); methoxyl 6.58, 6.65. In addition the spectrum integrated for eight protons in the region 5.3 - 6.5τ (H_2-H_5, $H_{2'}$-$H_{5'}$) and for four protons in the region 7.15 - 8.0τ ($-CH_2-CH_2-$). Further support for the "mixed dimer" structure postulated for XLVII was obtained by comparing the mass spectrum of the trimethylsilyl derivative of the "mixed dimer", XLVII, with the mass spectra of the trimethylsilyl derivatives of the "glucose dimer", V, and the "galactose dimer", XXXI, as shown in Fig. 32. In Fig. 32 only the more intense peaks are shown; however, the minor peaks corresponded equally well with only intensity differences between the three spectra.

DISCUSSION

Initially an investigation was made into the effect of ultraviolet light on methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I) in an aqueous solution. Compound I is readily available through a displacement reaction on methyl 6-O-p-tolylsulfonyl-α-D-glucopyranoside following a published method (5, 26). The compound was irradiated in the quartz apparatus shown in Fig. I using an unfiltered, medium pressure, Hanovia 250 W lamp. In order to filter out any 1849 Å radiation which could photolyse water molecules (40) to give hydrogen and hydroxyl radicals the apparatus was designed with approximately 1 cm of cooling water (41) between the lamp and the solution to be photolysed. The light emitted by the lamp in the 2537 Å region ensured strong radiation at the wavelength (2520 Å) absorbed by the carbon-iodine bond. By means of the stopcock in the base of the apparatus nitrogen was bubbled through the solution to flush out oxygen and to stir the solution. This stopcock was also used to collect samples from a reaction without interrupting irradiation of the solution. Solutions containing up to 4% (w/v) of methyl 6-deoxy-6-iodo-α-D-glucopyranoside were used in various experiments.

When a solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside in pure water was irradiated the solution rapidly became acidic, but no iodine was liberated. It was

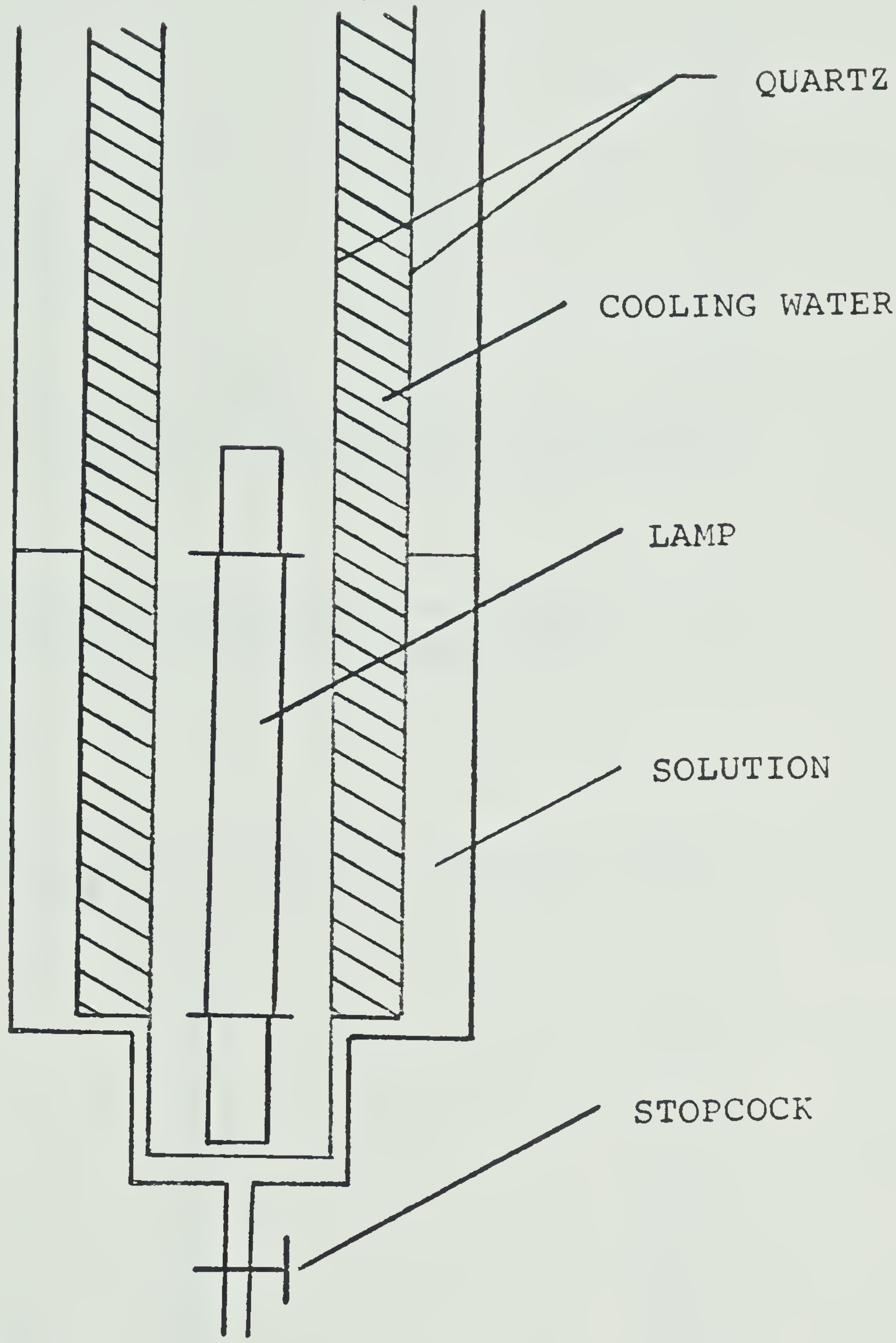


FIG. 1. Diagram of photolysis apparatus

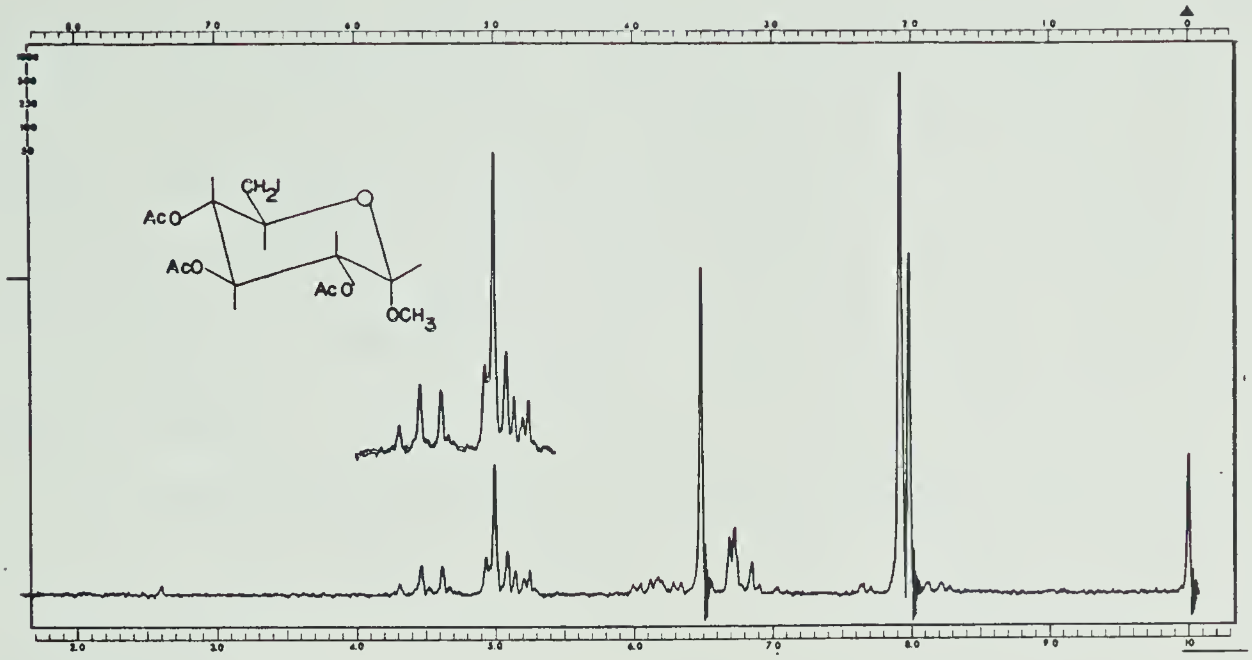


FIG. 2. P.m.r. spectrum (60 Mc.p.s.) of methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside (deuteriochloroform)

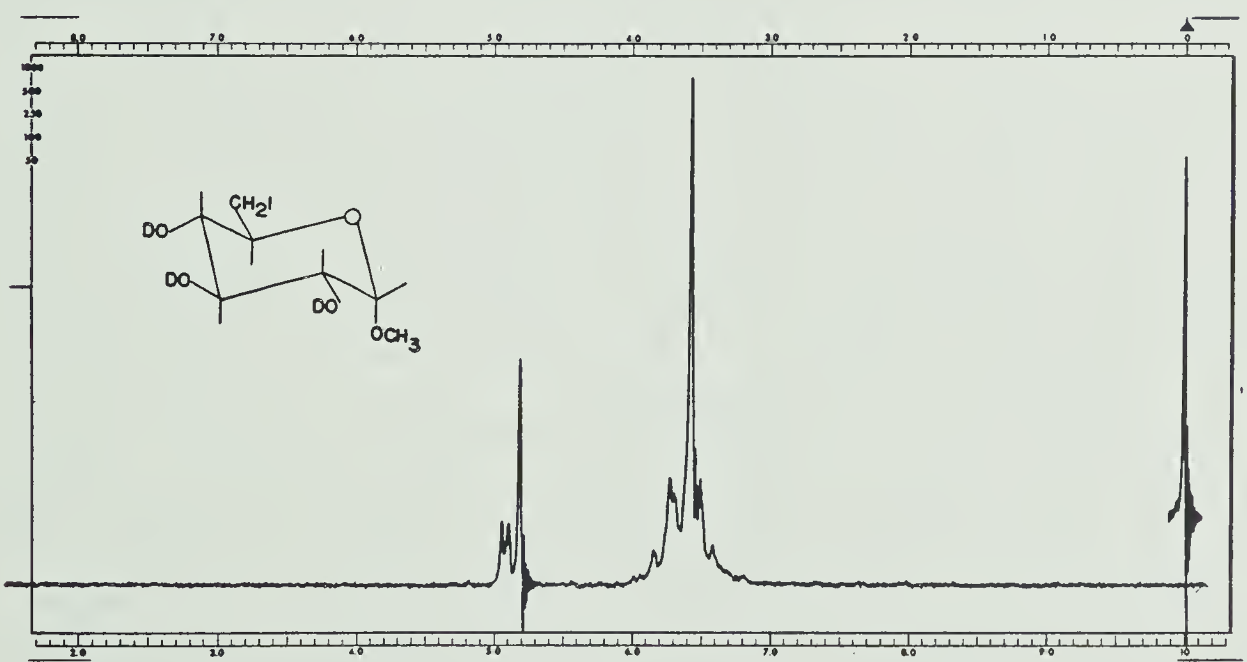


FIG. 3. P.m.r. spectrum (60 Mc.p.s.) of methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I) (deuterium oxide)

decided to buffer the solution by adding sodium bicarbonate and to follow the reaction by measuring the quantity of sodium bicarbonate neutralised, while at the same time titrating aliquots with silver nitrate using dichlorofluorescein as the indicator to determine the quantity of iodide present in the solution. A further measure of change in the irradiated solution was obtained by observing the change in the optical rotation of the solution when it was irradiated.

When an aqueous solution 0.12 molar in methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I) and 0.2 molar in sodium bicarbonate was irradiated it was apparent from samples analysed at intervals for iodide ion concentration that almost all of the iodocompound, I, had reacted after ten hr (Table II). Analysis of samples, irradiated for ten hr, showed that for each mole of I added initially to the solution, 1.11 mole of sodium bicarbonate had been neutralised. It was found that if samples from the solution, which had been irradiated for ten hr, were allowed to stand for twelve hr before titration the results were virtually unchanged. On the basis of the quantity of unreacted starting material isolated when the procedure was repeated with isolation of the products it was apparent that after ten hr irradiation 88% of I had reacted. Calculated on this basis each mole of I which reacted produced an average of 1.27 moles of acid.

A 0.12 M aqueous solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, without sodium bicarbonate, was irradiated and the reaction followed by titrating samples removed at intervals with sodium hydroxide. The formation of iodide was followed as before by titrating the neutralised solution with silver nitrate. After photolysis for six hours the solution became light yellow in colour and gave a positive test for iodine with starch. Although in both the buffered and unbuffered solutions the rate of production of acid appeared to be the same, in the unbuffered solution, the rate of formation of the iodide was a little slower, but the change in the optical rotation was greater (Table I).

To show that the acidity produced during the photolysis of I was due to processes arising out of the photolysis of the carbon-iodine bond, a solution containing methyl α-D-glucopyranoside in place of I was photolysed. After eight hours photolysis, for each mole of methyl α-D-glucopyranoside present originally, 0.016 moles of acid was produced. The p.m.r. spectrum of the product was indistinguishable from that for pure methyl α-D-glucopyranoside.

An aqueous solution (220 ml) of methyl 6-deoxy-6-iodo-α-D-glucopyranoside (26.4 mmole) and sodium bicarbonate (46.3 mmole), stirred by a stream of nitrogen was photolysed for ten hours. The solution was a light yellow colour, but gave a negative test for iodine. Concentration in vacuo yielded a syrup whose p.m.r. spectrum (Fig. 4) showed signals

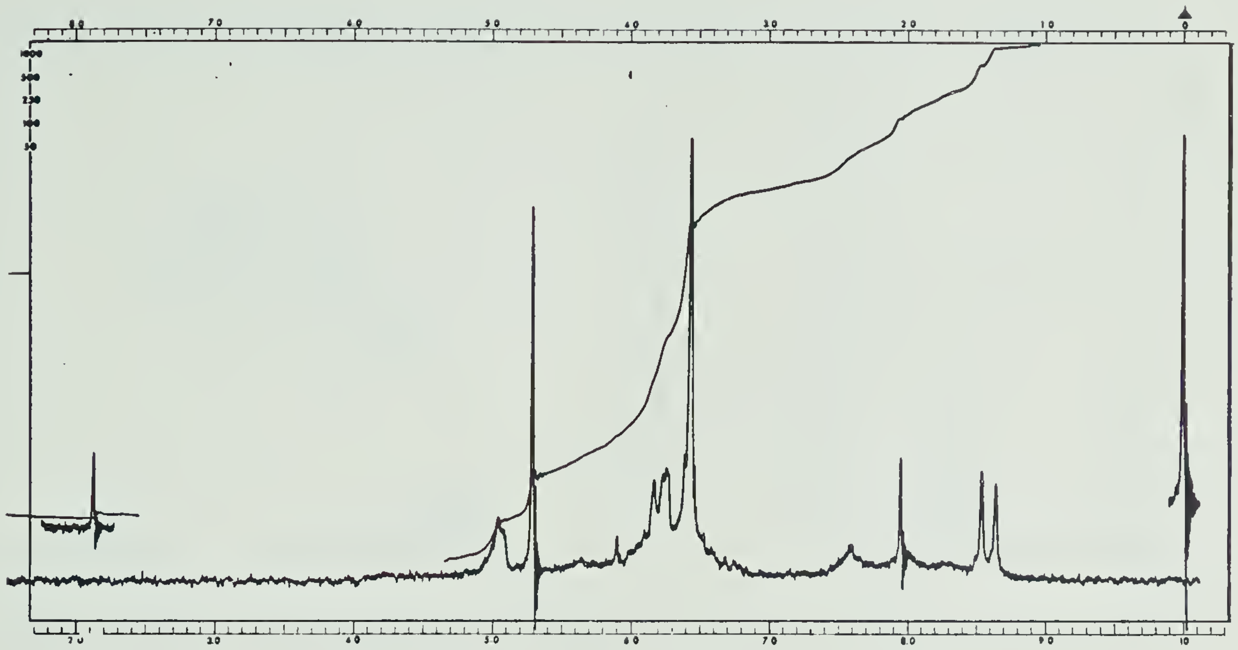


FIG. 4. P.m.r. spectrum (60 Mc.p.s.) of crude product from photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside (deuterium oxide)

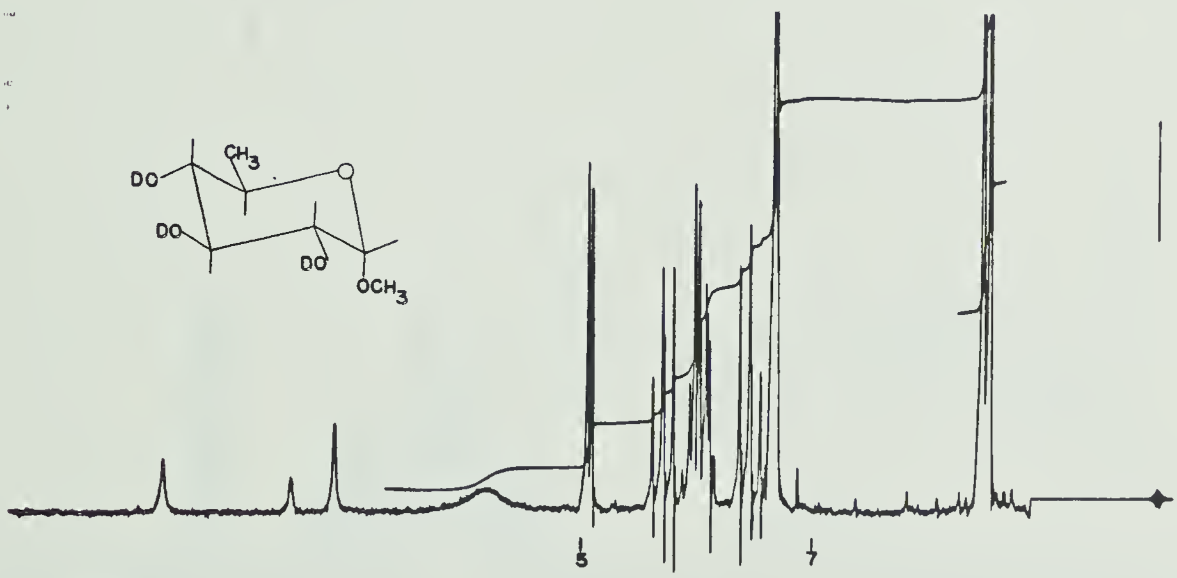


FIG. 5. P.m.r. spectrum (100 Mc.p.s.) of methyl 6-deoxy-α-D-glucopyranoside (III) (deuteriopyridine)

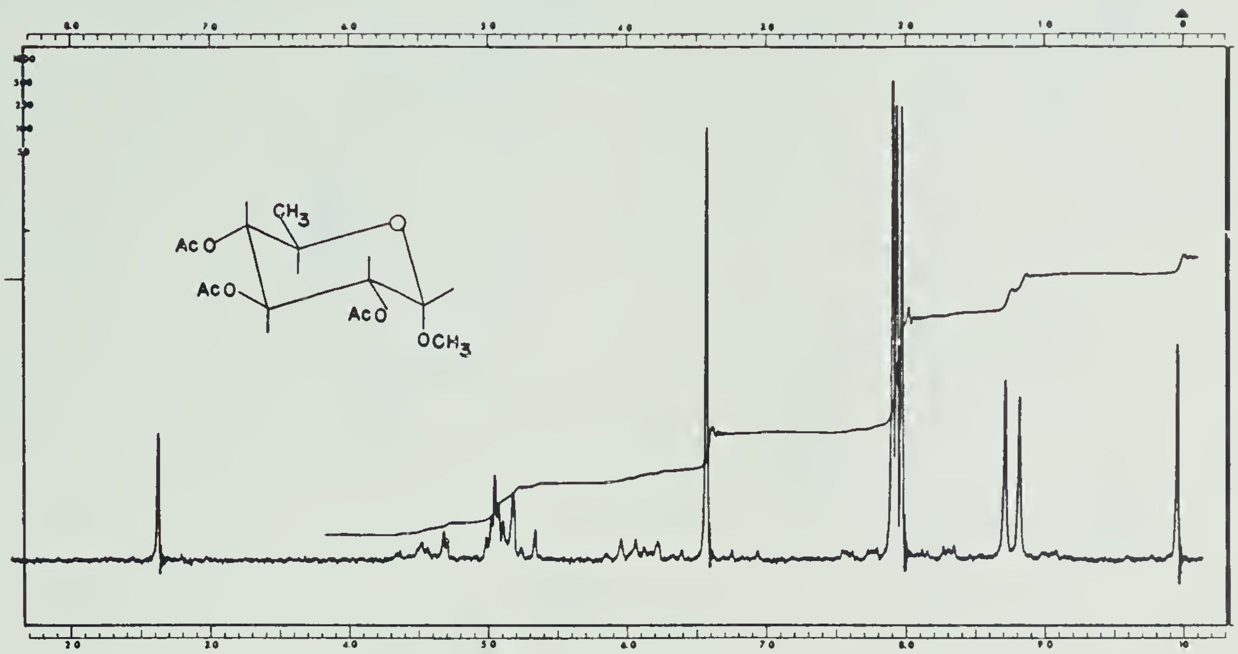


FIG. 6. P.m.r. spectrum (60 Mc.p.s.) of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside (IV) (deuteriochloroform)

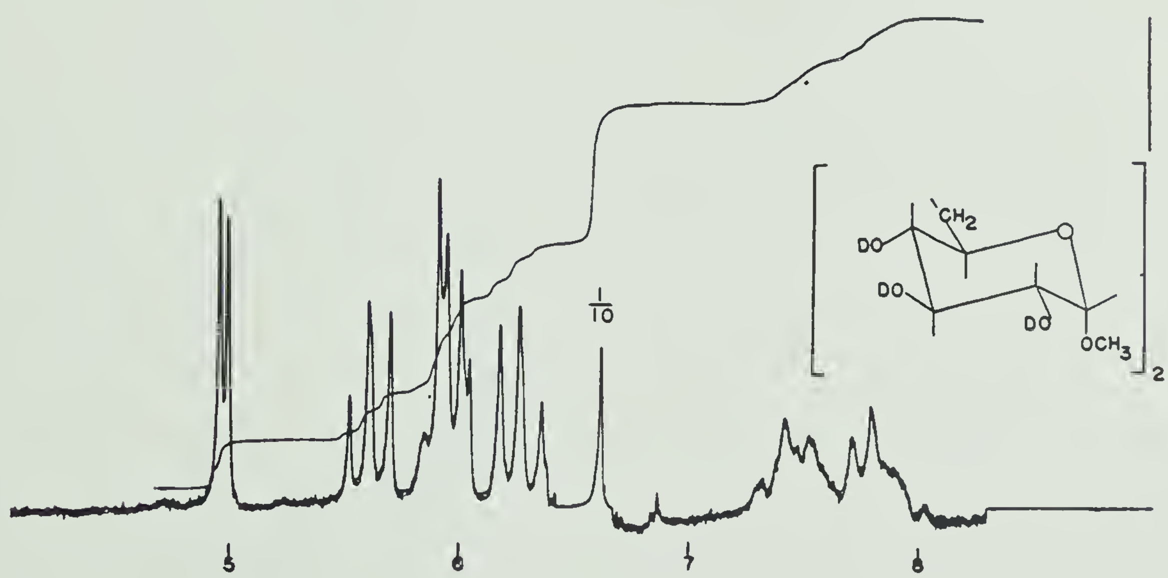
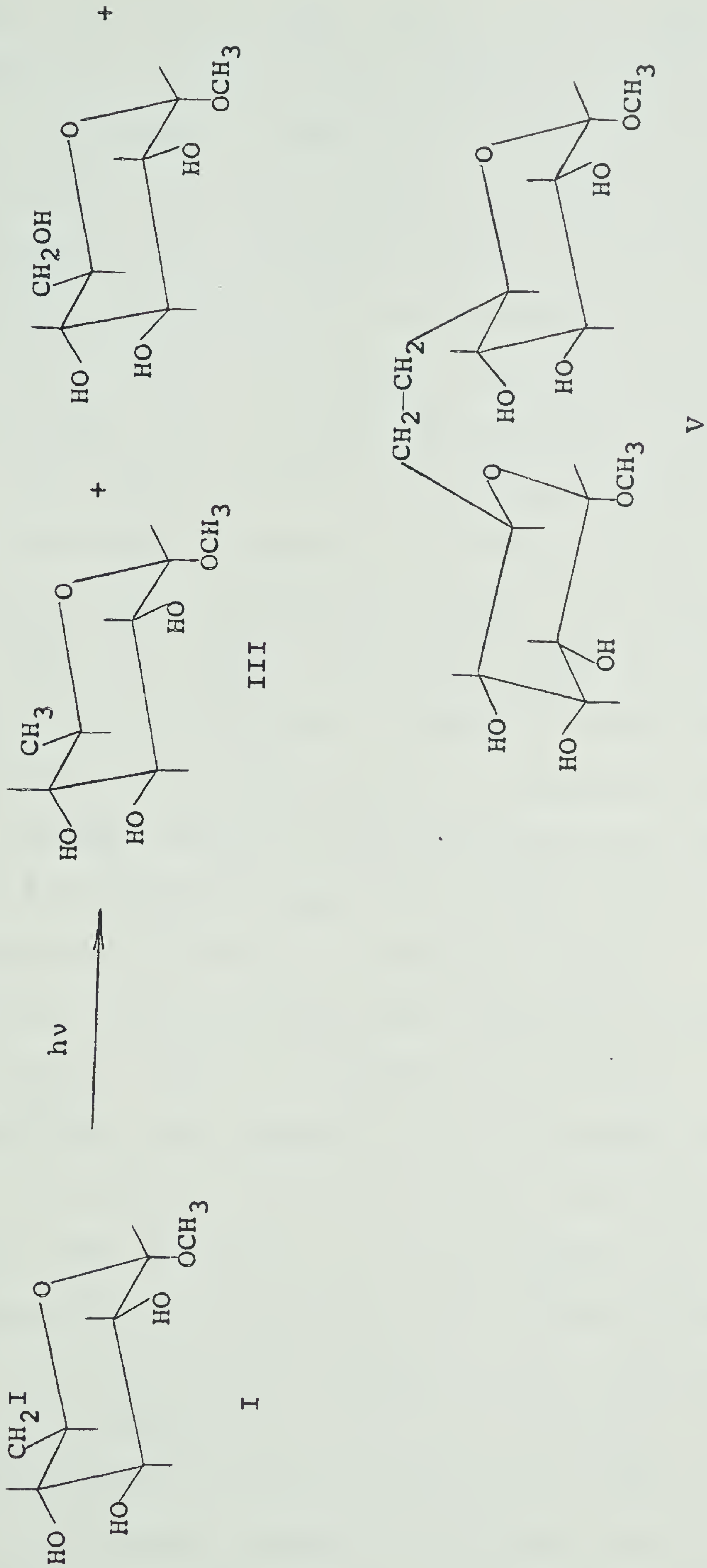


FIG. 7. P.m.r. spectrum (100 Mc.p.s.) of methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside (V) (deuteriopyridine)



I

III

V

in the region 7.4 - 8.7τ as well as 5.0 - 6.8τ. Separation of the products by n-butanol-water partition chromatography on a Celite column gave, in addition to starting material (I) (12% recovered) and sodium iodide, two other compounds. These two compounds when examined by paper chromatography showed extensive streaking which was eliminated by passing aqueous solutions of the two compounds through columns of ion-exchange resins. The two crystalline products isolated in this way were, methyl 6-deoxy-α-D-glucopyranoside (III), yield 23.1%, and methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside (V), hereafter called "the dimer, V", yield 5.8%. These yields are based on unrecovered starting material. Compound III was shown to be methyl 6-deoxy-α-D-glucopyranoside by comparison with an authentic sample prepared by hydrogenation of I. The structure of V was apparent from the following data.

Elemental anlysis and a molecular weight determination on V gave results which indicated the molecular formula $C_{14}H_{26}O_{10}$. The p.m.r. spectrum of V (Fig. 7), measured in deuteriopyridine after exchanging with deuterium oxide, was analysed for protons with the following chemical shifts (τ value): H_1, 4.98 (doublet); H_2, 5.98 (quartet); H_3, 5.61 (triplet); H_4, 6.27 (triplet); H_5, ∿5.95 (hidden multiplet); $H_{6,6'}$, 7.25 - 8.0 (multiplet); methoxyl, 6.62. Coupling constants (c.p.s.) were: $J_{1,2}$, 3.5; $J_{2,3}$, 9.5; $J_{3,4}$, 8.5; $J_{4,5}$, 9.5. Integration of the spectrum showed seven other protons for each methoxyl group. On this basis the structure

of the dimer V must consist of two identical portions since each of the above signals must represent two equivalent protons. A comparison of chemical shifts and coupling constants of the ring protons (H_1 - H_5) above with those obtained for methyl 6-deoxy-α-D-glucopyranoside (III) (Table VII) shows little difference between the two. This evidence suggests that compound V consists of two methyl 6-deoxy-α-D-glucopyranoside molecules linked together by a carbon-carbon bond at carbon-6.

TABLE VII

P.M.R. Parameters for Methyl 6-deoxy-α-D-glucopyranoside, III, and Methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside, V.

	H_1	H_2	H_3	H_4	H_5	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
III	5.08	6.05	5.70	6.46	6.00	3.5	9.5	8.5	9.5
V	4.98	5.98	5.61	6.27	5.95	3.5	9.5	8.5	9.5

The reaction of the dimer, V, with excess sodium periodate was measured by dissolving 38 mg of V in a buffered solution of sodium periodate and analysing aliquots removed at intervals by the method of Mueller and Friedberger (36). It was apparent from the results that each mole of the dimer, V, consumed four moles of sodium periodate. This is the result

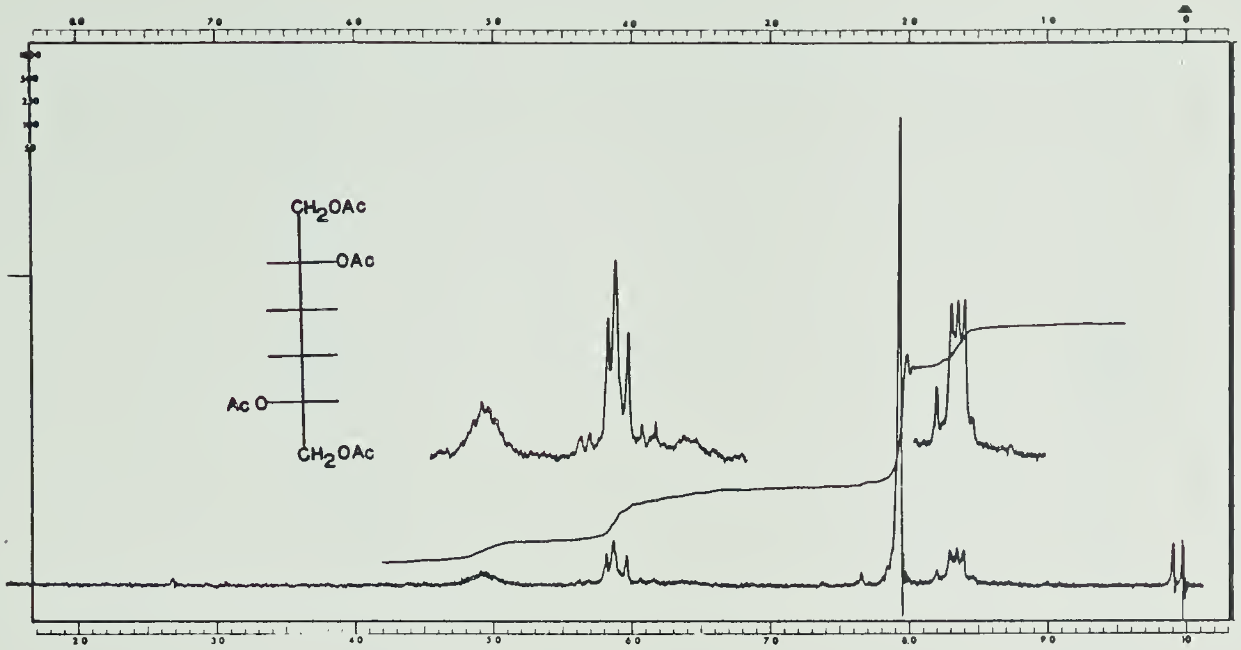


FIG. 9. P.m.r. spectrum (60 Mc.p.s.) of 3,4-dideoxy-tetra-O-acetyl-L-threo-hexitol (VI) (deuteriochloroform)

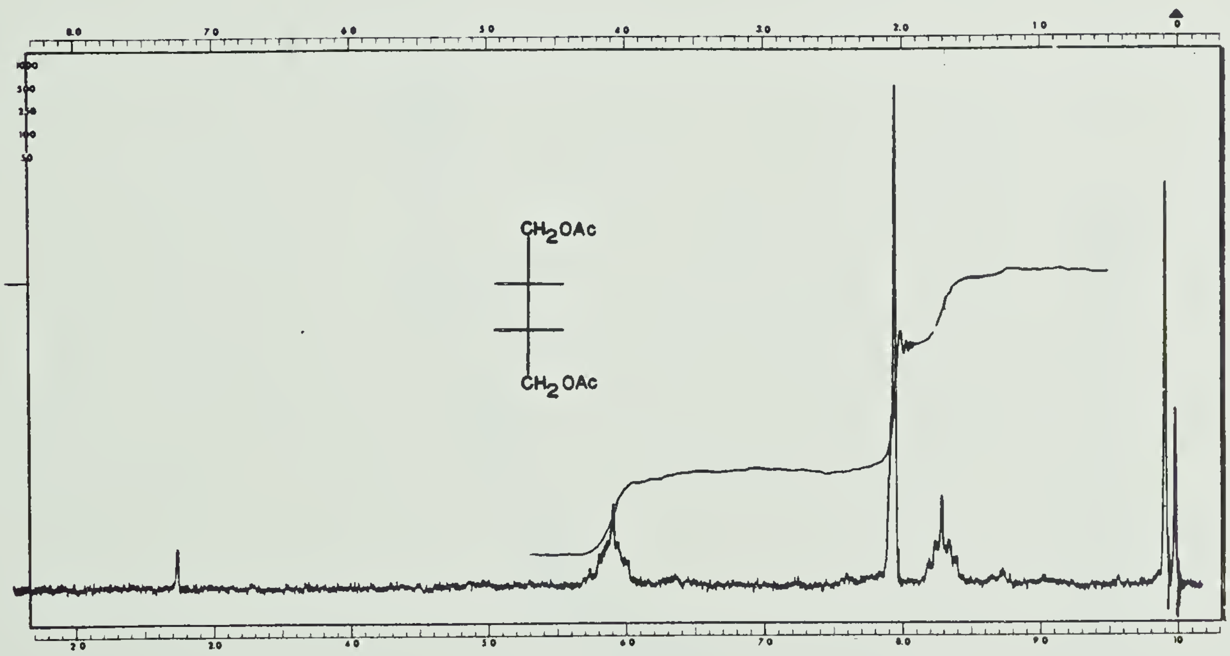


Fig. 10. P.m.r. spectrum (60 Mc.p.s.) of 1,4-butanediol diacetate (VIII) (deuteriochloroform)

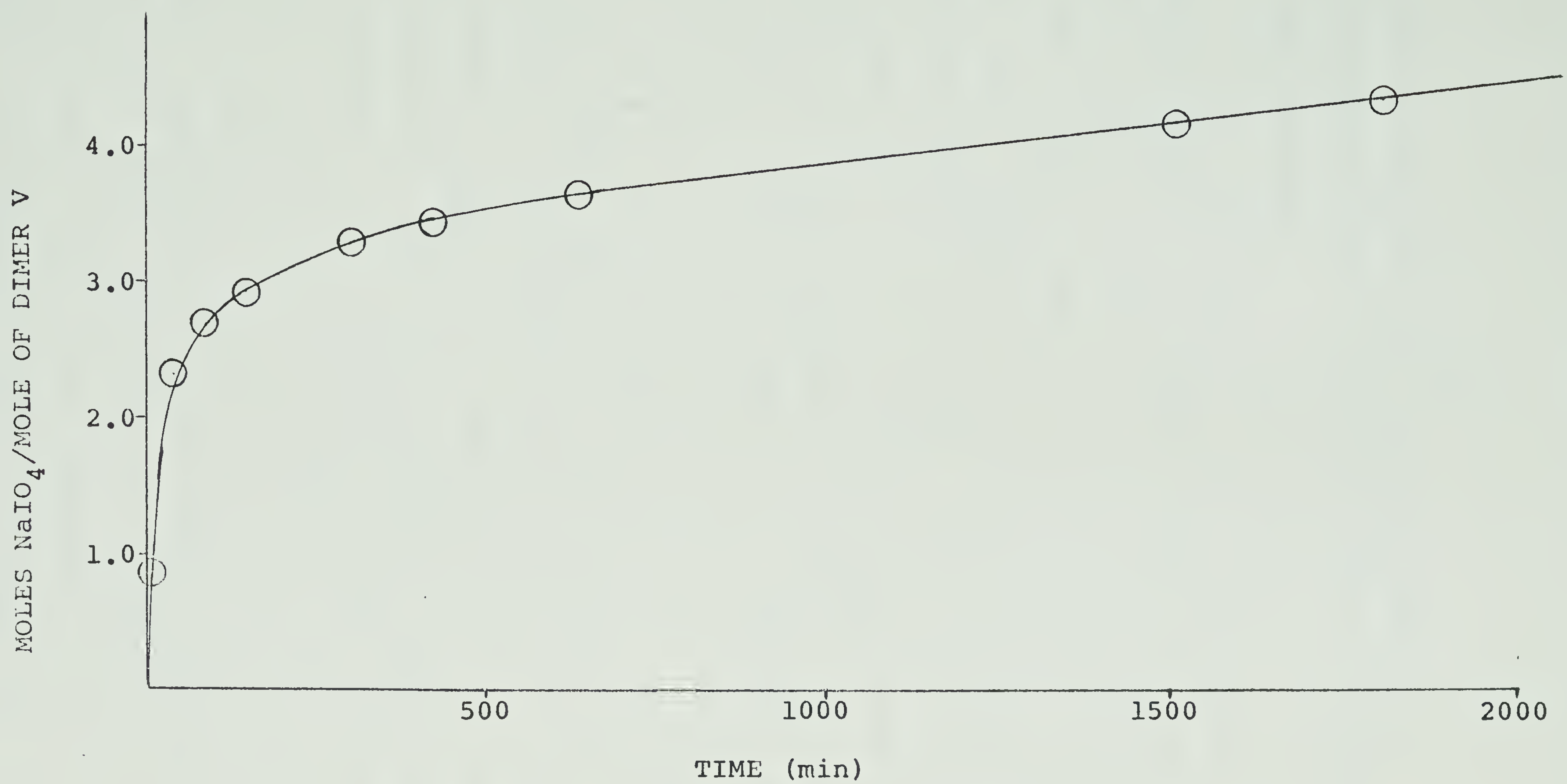
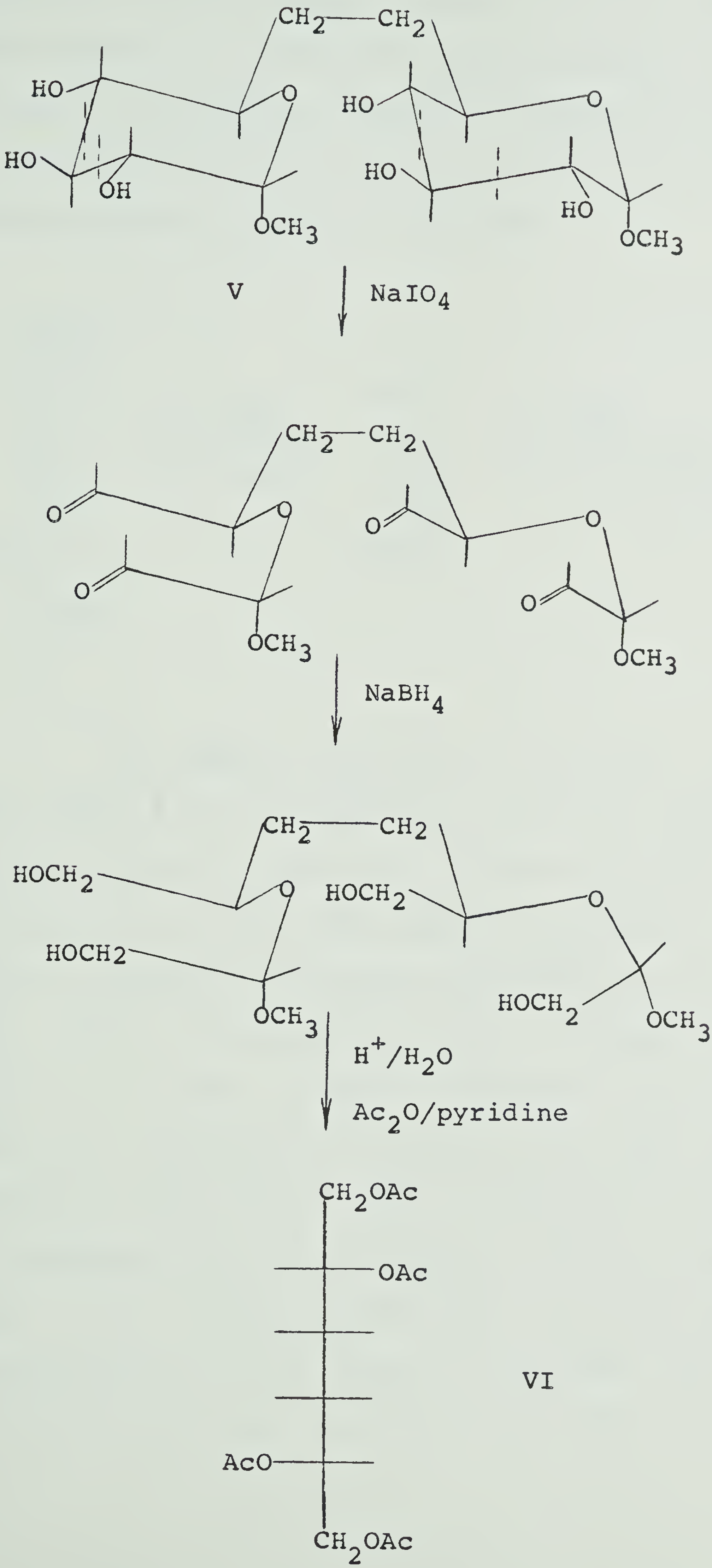


FIG. 8. Plot of sodium periodate oxidation of methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside (V)

which would be expected since a mole of methyl α-D-glucopyranoside consumes two moles of sodium periodate under these conditions.

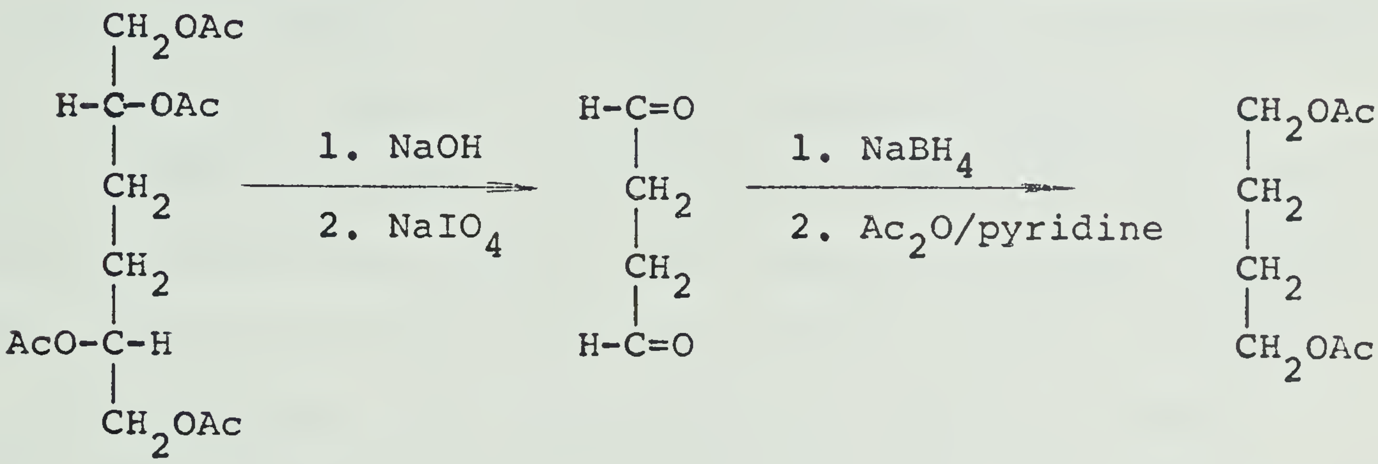
To show that compound V was in fact a dimer linked by a carbon-carbon bond an aqueous solution of V was reacted with excess sodium periodate and the resulting aldehyde groups were reduced by adding sodium borohydride to the solution. Acetal linkages were hydrolysed by heating the solution with Amberlite IR 120 (H^+) resin. The resulting alcohol, postulated to be 3,4-dideoxy-L-threo-hexitol, was acetylated with acetic anhydride in pyridine in the usual manner to give a syrup, VI, whose p.m.r. spectrum in deuteriochloroform (Fig. 9) showed protons with the following chemical shifts (τ value): 4.95, multiplet (IH); 5.8 - 6.0, multiplet (2H); 7.92, singlet (6H); 8.25 - 8.50, multiplet (2H). These results are compatible with the structure 3,4-dideoxy-tetra-O-acetyl-L-threo-hexitol postulated for VI. Compound VI was deacetylated with sodium hydroxide, cleaved with sodium periodate and the resulting dialdehyde was reduced with sodium borohydride to the alcohol VII, whose p.m.r. spectrum in deuterium oxide was identical to that of 1,4-butanediol. Acetylation of VII with acetic anhydride and pyridine gave a syrup, VIII. The p.m.r. spectrum of VIII in deuteriochloroform (Fig. 10) was identical to the p.m.r. spectrum of 1,4-butanediol diacetate measured under the same



V

VI

conditions. Both compounds showed the same retention time when examined by gas-liquid chromatography. Carbons 2 and 3 of the 1,4-butanediol isolated by degradation of the dimer V, are considered to be the two carbons (carbons 6,6') linking the two halves of the dimer.



VI VIII

The dimeric structure of the dimer V requires that compound VI be asymmetric and hence probably optically active. Although a specific rotation of $[\alpha]_D^{25}$ + 3°was obtained for VI, when the specific rotation of compound XXXIII, obtained by analogous degradation of the galactose dimer, XXXI, was measured it gave a different result, $[\alpha]_D^{25}$ + 0.3°. These different rotations obtained for VI and XXXIII are considered to be due to the small amount of impurity present which could be detected by examining the two compounds by t.l.c. Moreover, the p.m.r. spectrum (Fig. 7) of V clearly establishes the α-D-glucopyranose configuration of both halves of the dimer thus ruling out the possibility that one half of the dimer underwent

inversion at carbon-5 to achieve the β-L-idopyranoside configuration. Also the identical p.m.r. and I.R. spectra of compounds VI and XXXIII together with their identical chromatographic behaviour leaves no doubt that they are the same compound.

Acetylation of the dimer, V, with acetic anhydride in pyridine yielded a crystalline compound, IX whose analysis was consistant with the molecular formula $C_{26}H_{38}O_{16}$. The p.m.r. spectrum of IX in deuteriochloroform (Fig. 11) could not be analysed as a first order spectrum; however, signals were obtained with the following chemical shifts (τ value): H_3, 4.59 (triplet, 1H); H_1, H_2 and H_4, 5.05 - 5.3 (3H); H_5, 6.05 - 6.35 (multiplet, 1H); $H_{6,6'}$, 8.3 - 8.4 (multiplet, 2H); methoxyl, 6.63 (3H); acetyl, 7.95, 7.99, 8.02 (9H). Irradiation of the multiplet at 8.3 - 8.4τ ($-CH_2-CH_2-$) caused the multiplet at 6.1 - 6.4τ, assigned to H_5, to collapse to a doublet with a spacing of 9.5 c.p.s. These p.m.r. assignments are in accord with the structure, methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside hexa-acetate proposed for IX. Confirmation of these assignments was obtained when the 1-deuterio analogue of IX was isolated in a later experiment. In this case H_2 was observed as a doublet with a spacing of 10 c.p.s. at 5.17τ and H_4 was observed as a triplet with a spacing of 9.5 c.p.s. at 5.15τ.

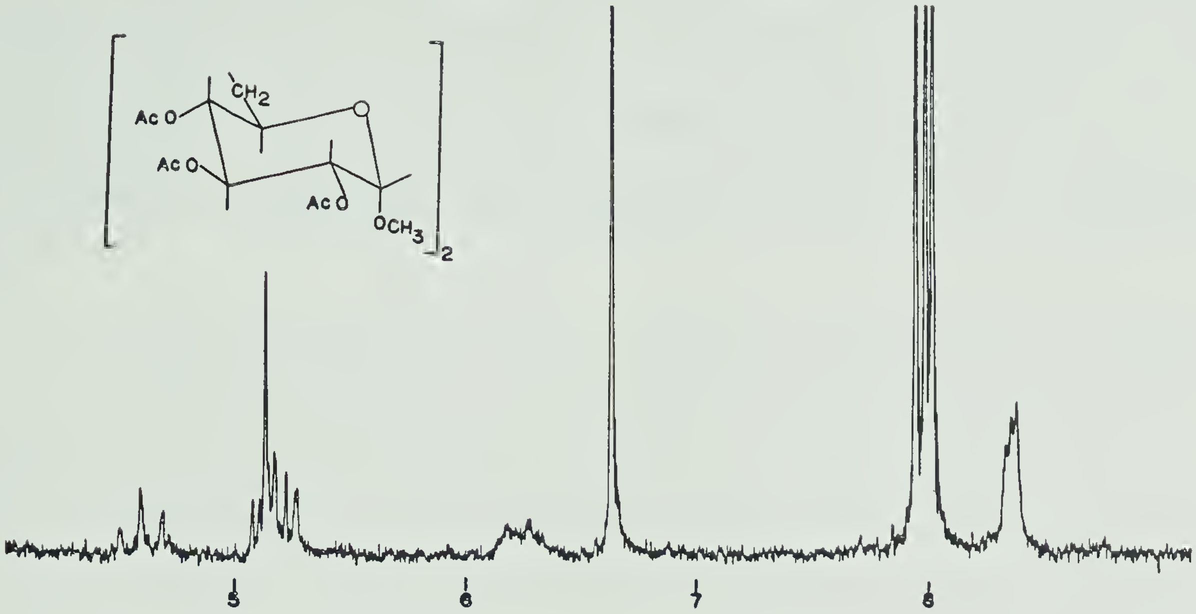


FIG. 11. P.m.r. spectrum (100 Mc.p.s.) of methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside]-6-yl)-α-D-glucopyranoside hexa-acetate (IX) (deuteriochloroform)

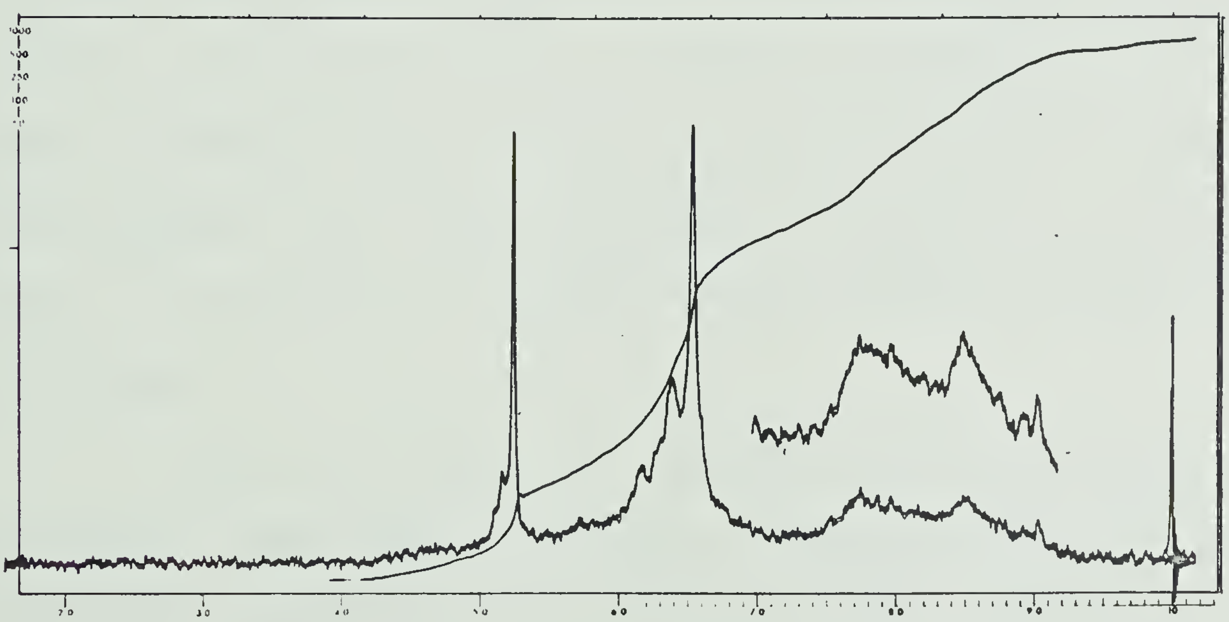


FIG. 12. P.m.r. spectrum (60 Mc.p.s.) of XII (deuterium oxide)

The Celite column used to separate the products from the photolysis reaction was finally eluted with water to give after concentration a dark syrup, X, which was not identified but appeared to contain at least one carboxylic acid.

The photolysis of an aqueous solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside in the presence of sodium bicarbonate was repeated using the same quantities of reagents and the same conditions as were used previously. Separation of the products on a Celite column as before gave similar yields of the 6-deoxy compound III, and the dimer V. Finally elution of the Celite column with water gave on concentration a dark syrup which was passed as an aqueous solution through a column of Amberlite IR 120 (H^+) to remove any sodium bicarbonate. Concentration <u>in vacuo</u> yielded a dark syrup equal to 30% of the weight of reacted methyl 6-deoxy-6-iodo-α-D-glucopyranoside minus the weight of the iodine atom. This material was similar to the dark syrup, X, obtained by elution of the previous Celite column with water.

Since the identified organic products account for only 29% of the amount of methyl 6-deoxy-6-iodo-α-D-glucopyranoside consumed in the reaction, other separation techniques were investigated. Using the same concentration of reagents as before, an aqueous solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, buffered with sodium bicarbonate,

was photolysed for ten hours. Concentration *in vacuo* of the reaction mixture gave a syrup which was acetylated by dissolving it in a mixture of acetic anhydride and pyridine. An attempt was made to separate the resulting syrup on a silicic acid column eluted successively with chloroform and chloroform-ethanol. In this way methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside and methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside could be separated. Deacetylation of a further fraction followed by deionisation with ion-exchange resins, yielded the dimer V. Elution of the silicic acid column with 1% (v/v) ethanol-chloroform yielded a syrup, XI, which could not be crystallised and was found to have a molecular weight of 800. Deacetylation of compound XI yielded a syrup, XII, which darkened on standing. The p.m.r. spectrum of XII (Fig. 12) in deuterium oxide, which was similar to the p.m.r. spectrum of compound X, was very poorly resolved, but extensive signals in the regions 7.5 - 9.0τ suggested the presence of a chain of methylene protons. Absorptions at 1630 cm^{-1} and 1710 cm^{-1} in the I.R. spectrum of XII suggested that it contained a carboxylic acid group. To explain a molecular weight of 800 for XI it is necessary to involve at least three molecules of I in the formation of one molecule of XI. Attempts to degrade compound XII by acid hydrolysis of acetal linkages provided no useful new information.

Whistler and Durso (43) in 1950 described how saccharides could be separated into classes according to the degree of polymerisation, that is, monosaccharides, disaccharides, trisaccharides and so on. The procedure involved graded elution by aqueous ethanol from a carbon-Celite column. Graded elution with aqueous ethanol has found many uses including the separation of some uronic acids (44). For separation of more complex mixtures Alm and coworkers (45) introduced the technique of gradient elution by aqueous ethanol from carbon-Celite columns. The difference between the two is that in the case of gradient elution the concentration of ethanol increases in a linear manner. A carbon-Celite column was prepared using the procedure described by Whistler and BeMiller (24), the column being deactivated with concentrated hydrochloric acid before use.

An aqueous solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, buffered with sodium bicarbonate, was photolysed for ten hours using the same conditions as previously. Concentration of the photolysed solution yielded a syrup which was applied as a 10% aqueous solution to the top of the carbon-Celite column. The column was eluted first with water and was then subjected to gradient elution using aqueous ethanol. Elution of compounds from the column was followed by measuring the optical rotations of the fractions (25 ml) collected. This procedure was greatly facilitated by the use of an automatic polarimeter.

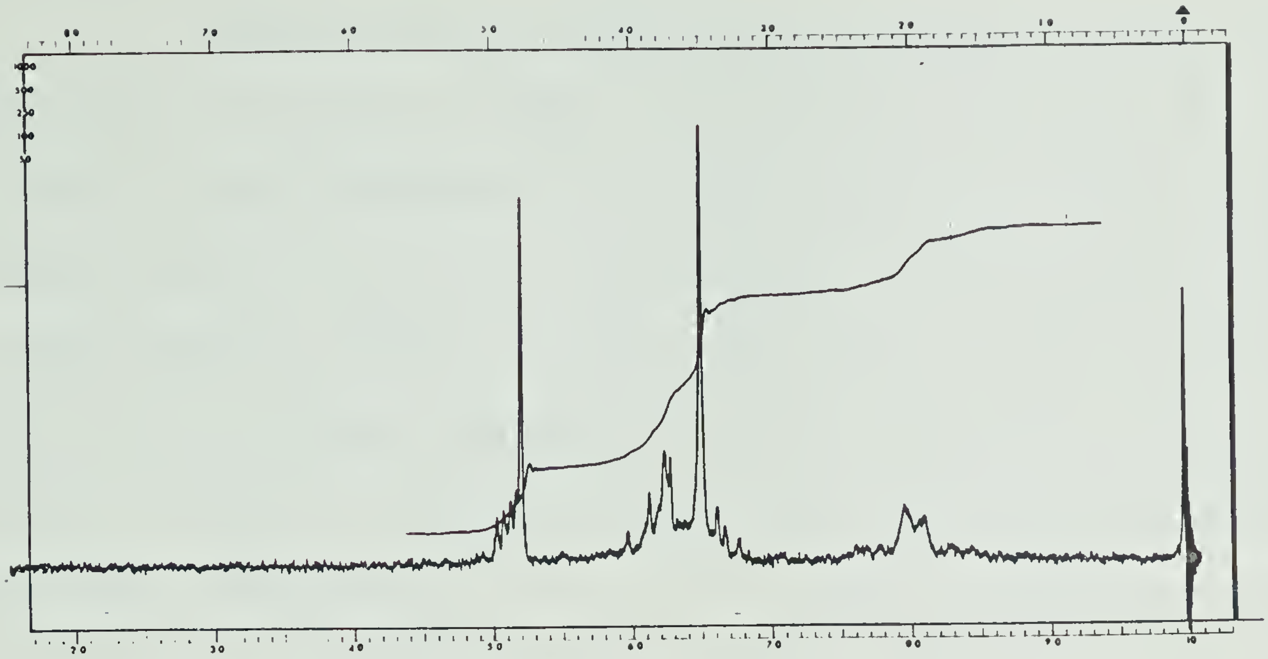


FIG. 13. P.m.r. spectrum (60 Mc.p.s.) of XIII (deuterium oxide)

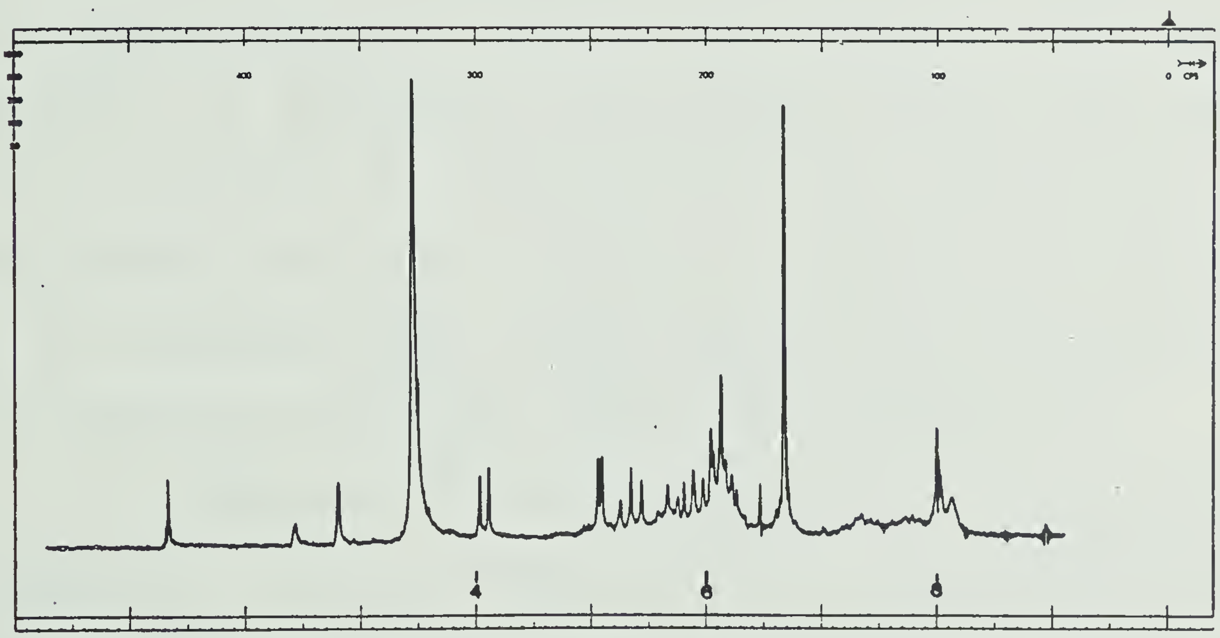


FIG. 14. P.m.r. spectrum (100 Mc.p.s.) of XIII (deuteriopyridine)

Carbon-Celite column chromatography proved to be the most successful method of separating the products, formed by the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, I, that was investigated. An advantage of the carbon-Celite column is that salts such as sodium iodide or sodium bicarbonate are eluted quickly from the column with water. Gradient elution of the column with aqueous ethanol gave six fractions, A, B, C, D, E, and F. Fraction F was shown to be unchanged methyl 6-deoxy-6-iodo-α-D-glucopyranoside, recovered 32%. Fractions A, B, E, and F respectively were shown to each consist of one compound and were identified as follows: methyl α-D-glucopyranoside, yield 3.7%; methyl 6-deoxy-α-D-glucopyranoside, III, yield 27%; dimer V, yield 5%. These yields are based on the quantity of starting material (I) consumed in the reaction (68%). This increase in the quantity of I recovered from the reaction mixture was considered to be due to material deposited from the water in the cooling jacket. These deposits were removed by rinsing the cooling jacket with dilute hydrochloric acid.

Fraction C when examined by t.l.c. showed three compounds. The major compound, XIII, was isolated as a chromatographically pure syrup representing a yield of ~3.5%. Decoupling experiments showed that the p.m.r. spectrum of XIII in deuteriopyridine (Fig. 14) contained two sets of three coupled protons; these are (τ value): H_1, 5.09 (doublet);

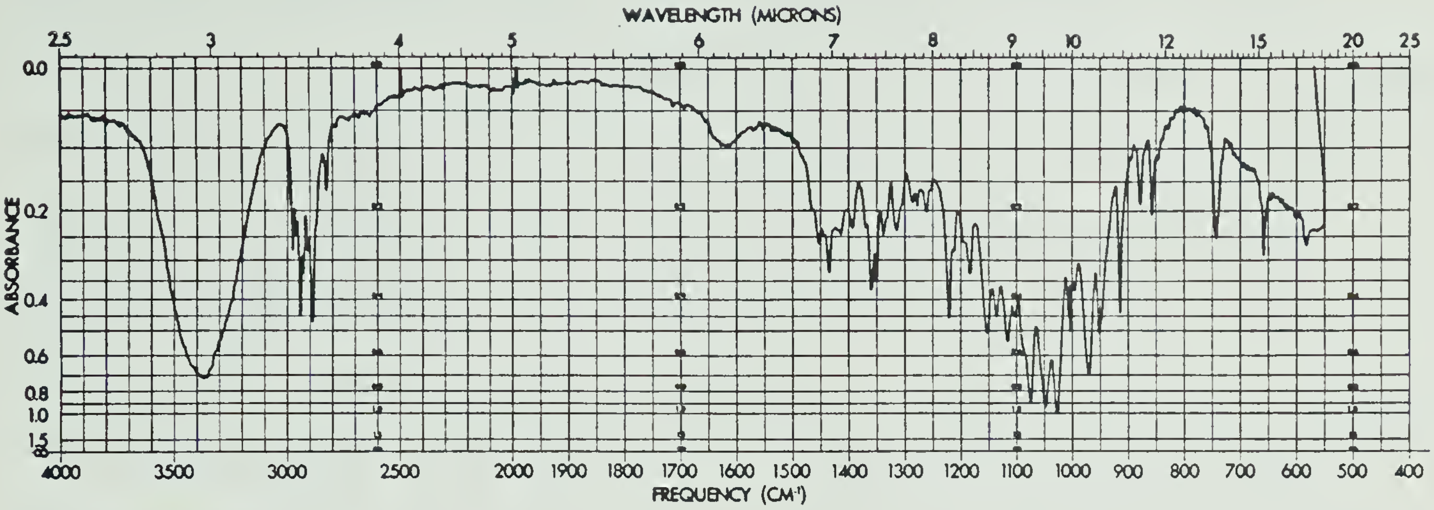


FIG. 15. I.R. spectrum (KBr disc) of XIV

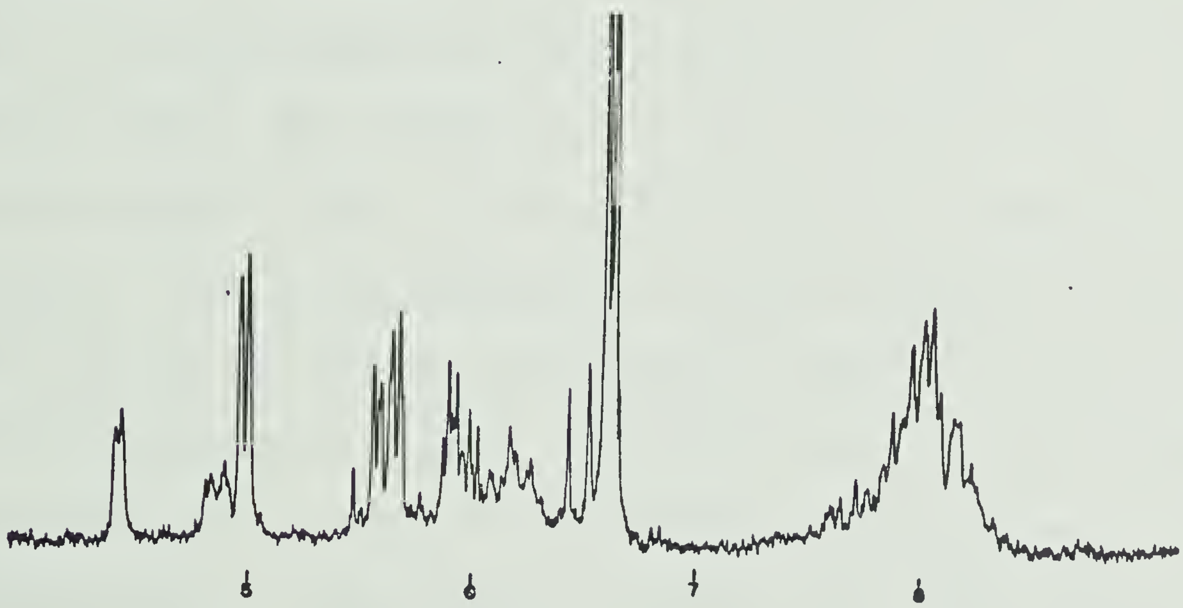


FIG. 16. P.m.r. spectrum (100 Mc.p.s.) of XIV (deuteriopyridine)

H_2, 6.21 (quartet); H_3, 5.58 (triplet); and $H_{1'}$, 4.08 (doublet); $H_{2'}$, 5.9 (triplet); $H_{3'}$, 5.36 (triplet). Coupling constants (c.p.s.) are: $J_{1,2}$, 3.5; $J_{2,3}$, 9.0; $J_{3,4}$, 8.0; $J_{1'2'}$, 7.5; $J_{2'3'}$, 9.0; $J_{3'4'}$, 9.0. Integration of the spectrum suggested four methylene protons in the region 7.1 - 8.2τ and one methoxyl group at 6.69τ. The I.R. spectrum of XIII showed an absorption at 1730 cm^{-1} with a weaker absorption at 1640 cm^{-1}. The molecular weight of XIII was determined to be 282. Although it was not possible to determine the structure of XIII it would appear to be formed from at least two molecules of the 6-iodo compound, I.

Examination of fraction D by t.l.c. revealed two compounds. A portion of the major compound (XIV) was obtained pure by crystallisation from n-propanol. The I.R. spectrum of XIV (Fig. 15) showed only a weak absorption at 1620 cm^{-1} in the region 1500 - 2000 cm^{-1}. The p.m.r. spectrum of XIV (Fig. 16) in deuteriopyridine showed signals in the region 4.4 - 6.5τ as well as two methoxyl signals at 6.60 and 6.63τ. In the region 7.5 - 8.4τ a multiplet was observed which was considered to be due to the presence of methylene protons. Integration of the spectrum showed that these three regions integrated in the ratio 5:2:3 respectively. It was not possible to determine the structure of XIV.

The crude weight of fractions A, B, C, D, and E when added together accounted for 72% of the methyl 6-deoxy-6-iodo-α-D-glucopyranoside which had undergone photolysis.

Further elution of the carbon-Celite column after elution of fraction E gave material whose p.m.r. spectrum was similar to the p.m.r. spectrum of the compounds eluted from the Celite column with water (compound X).

At this point in the research, it was evident that photolysis, as expected, initially provided the radical II. The formation of methyl 6-deoxy-α-D-glucopyranoside would then follow from this radical accepting a hydrogen atom from the hydrogen donor(s) (H-R) to produce the new radical(s) (R•). In order to demonstrate beyond doubt that the source of the hydrogen atom was not the water used as solvent, either by direct hydrogen abstraction leaving the hydroxyl radical or through some unknown mechanism to produce an iodine atom from the liberated iodide ion, a solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, I, in deuterium oxide, buffered with sodium bicarbonate was photolysed.

The methyl 6-deoxy-6-iodo-α-D-glucopyranoside and sodium bicarbonate were first exchanged with deuterium oxide. After photolysis the deuterium oxide solvent was freeze-dried and the p.m.r. spectrum of the liquid measured. By integrating with respect to a known quantity of added acetone it appeared that a ∿30% yield of methanol was obtained in the photolysis reaction.

Separation of the products by chromatography on a carbon-Celite column gave methyl 6-deoxy-α-D-glucopyranoside,

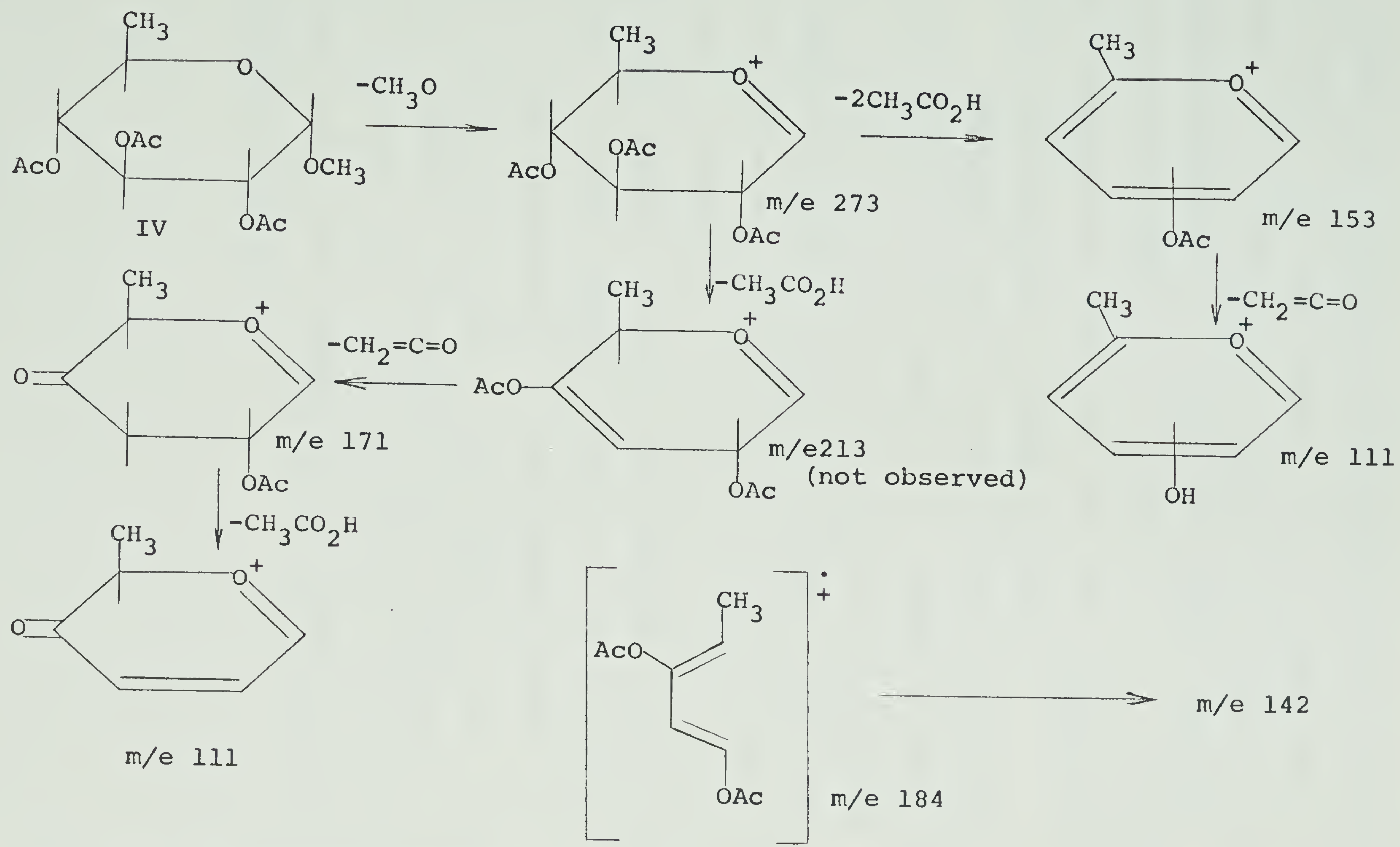
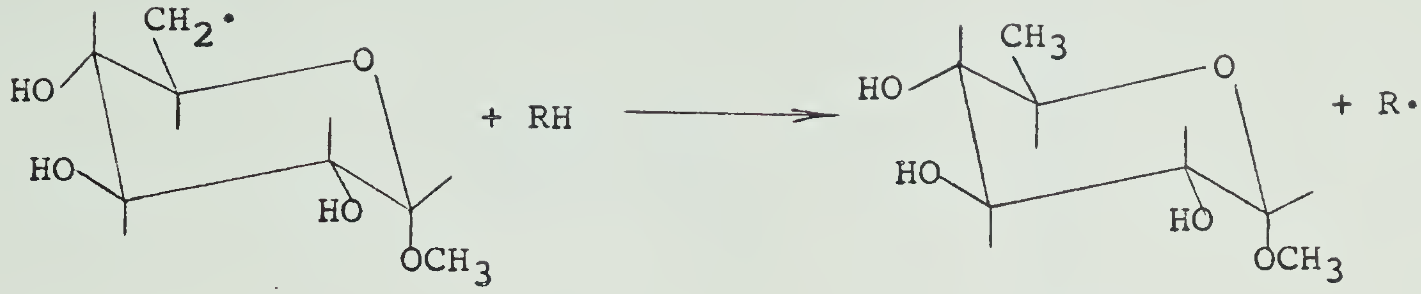


FIG. 17. Fragmentation pattern of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside

III, which was acetylated and examined by mass spectroscopy using an MS 9 Mass Spectrometer. Since no molecular ion was obtained it was necessary to compare the intensity of those fragments considered to contain the C-methyl group. By analogy with the fragmentation pattern of 1,2,3,4,-tetra-O-acetyl-6-deoxy-α-D-glucopyranose (46, 47), fragmentation patterns were postulated as shown in Fig. 17.

Additional proof for the structure of the ions m/e 184 and 142 was the presence of a metastable peak at 109.6. Also, the following peaks were explained: acetylium ion m/e 43, diacetyl oxonium ion m/e 103, triacetyl oxonium ion m/e 145, as well as m/e 157 and m/e 115 arising from carbons 2,3 and 4. A comparison of the ratio m : m+1 for these peaks, containing carbon-6, with the ratio obtained when the mass spectrum of a known sample of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside, IV, was examined showed that no extra deuterium was present in the sample. As well as proving that the hydrogen is abstracted from the carbohydrate solute this result also rules out any possibility that the formation of methyl 6-deoxy-α-D-glucopyranoside involves formation of a carbanion at carbon-6.



II III

The hydrogen-atom donor, RH, was therefore either starting material or/and products of its photochemical decomposition. A hydrogen atom considered likely to be abstracted from methyl 6-deoxy-6-iodo-α-D-glucopyranoside was the anomeric hydrogen at carbon-1. This view was supported by the singlet observed at 6.63τ, attributed to methanol, in the distillate from the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside in deuterium oxide. To test this hypothesis methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d, XV, was synthesised as described later in the Discussion.

Photolysis of an aqueous solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d, XV, in the presence of sodium bicarbonate followed by separation on a Celite column gave three fractions which, after deionising with ion-exchange resin, were shown to be; methyl 6-deoxy-α-D-glucopyranoside-1-d, yield 15.6%; methyl α-D-glucopyranoside-1-d, yield 2.7%; and methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside-1-d]-6-yl)-α-D-glucopyranoside-1-d (XVI) yield 9.3%. No methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d was recovered from the

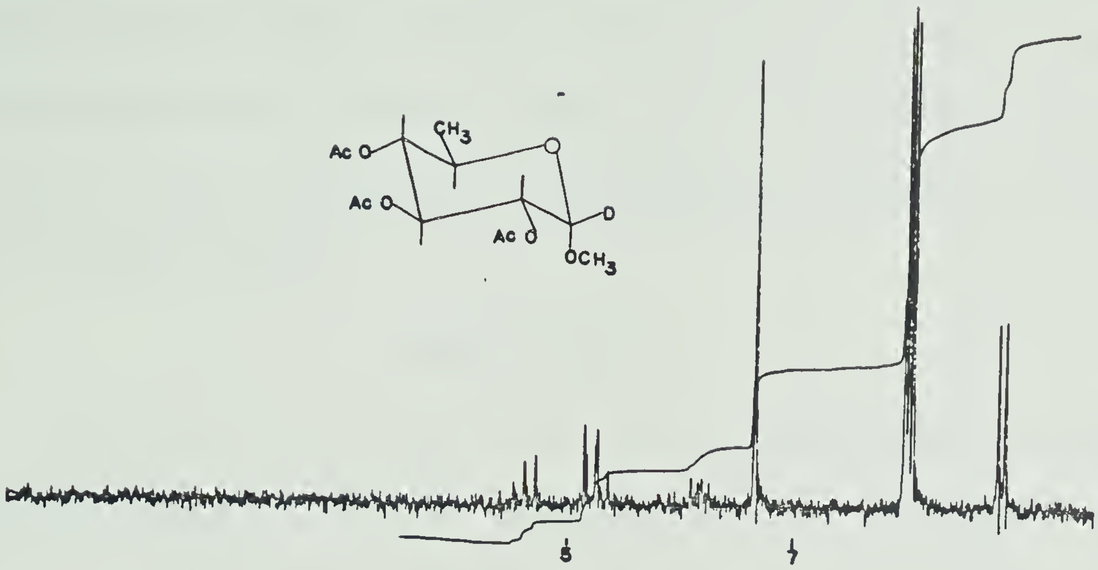


FIG. 18. P.m.r. spectrum (100 Mc.p.s.) of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside-1-d (XVII) (deuteriochloroform)

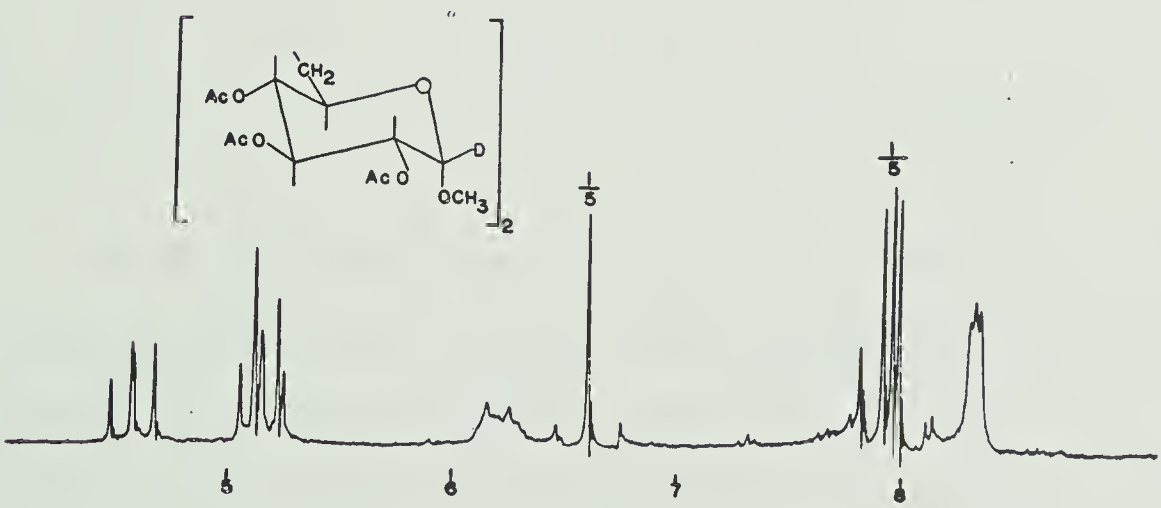


FIG. 19. P.m.r. spectrum (100 Mc.p.s.) of methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside-1-d]-6-yl)-α-D-glucopyranoside-1-d hexa-acetate (XVIII) (deuteriochloroform)

reaction product. The methyl 6-deoxy-α-D-glucopyranoside-1-d was acetylated to give methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside-1-d, XVII, whose p.m.r. spectrum in deuteriochloroform (Fig. 18) showed the chemical shifts (τ value) listed in Table VIII.

TABLE VIII

P.M.R. Parameters for Methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside-1-d (XVII) and Methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside-1-d]-6-yl)-α-D-glucopyranoside-1-d hexa-acetate (XVIII)

	H_2	H_3	H_4	H_5	H_6	methoxyl	acetyl
XVII	5.09	4.62	5.25	6.16	8.82	6.67	8.00, 8.04, 8.07
XVIII	5.17	4.58	5.15	∿6.2	∿8.3	6.61	7.92, 7.96, 7.99

When the mass spectrum of XVII, measured on the MS 9 Mass Spectrometer, was examined the fragments previously postulated to contain carbon-1, m/e 171, 153 and 111, were increased by one mass unit to m/e 172, 154 and 112, due to the replacement of hydrogen by deuterium at carbon-1. It was therefore considered that only by comparing the relative intensities of the m/e 142 and m/e 143 peaks, which did not contain carbon-1, would a true measure of the deuterium

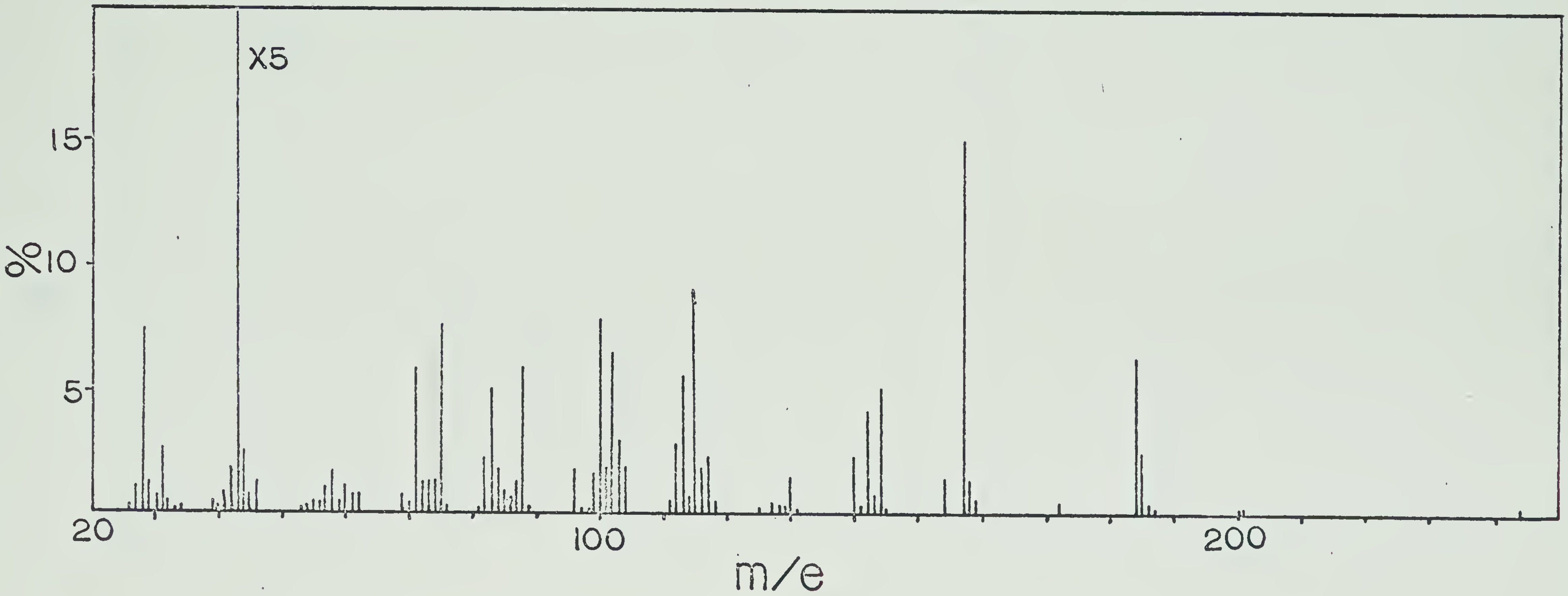


FIG. 20. Mass spectrum of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside-1-d (XVII)

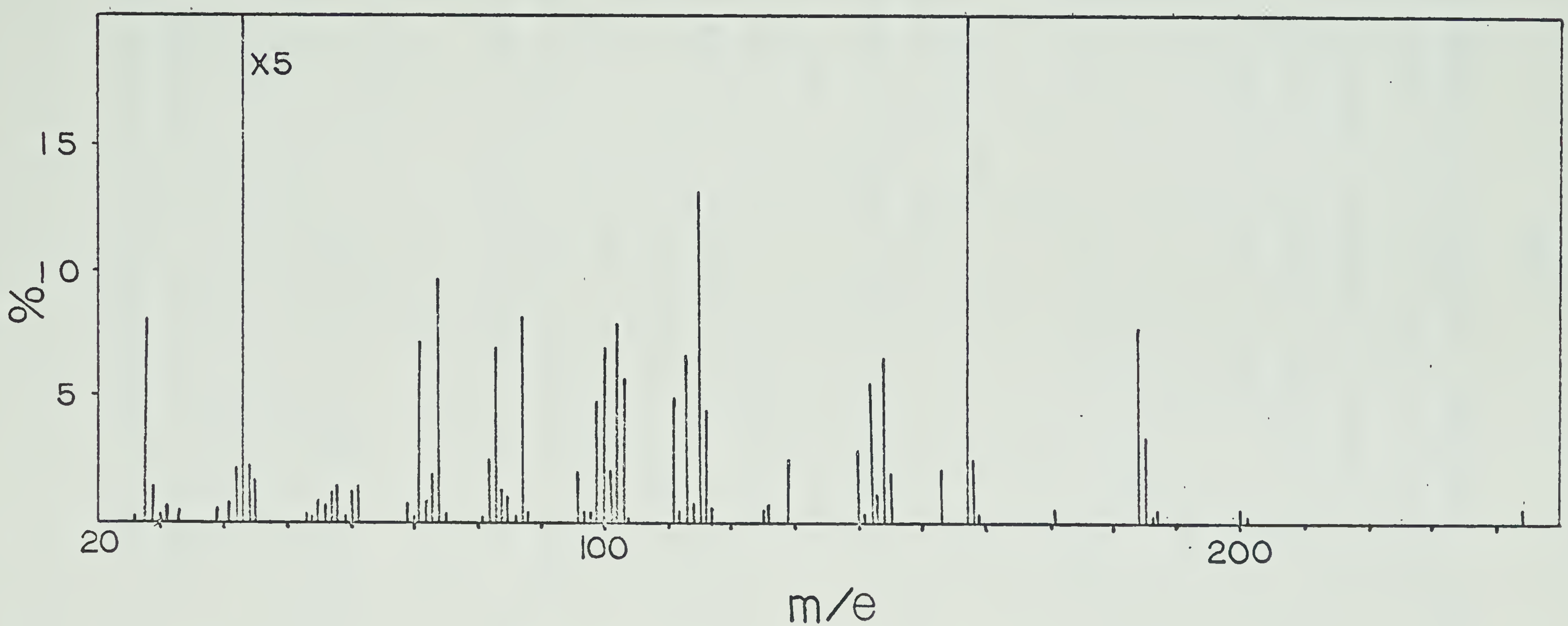


FIG. 21. Mass spectrum of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside (IV)

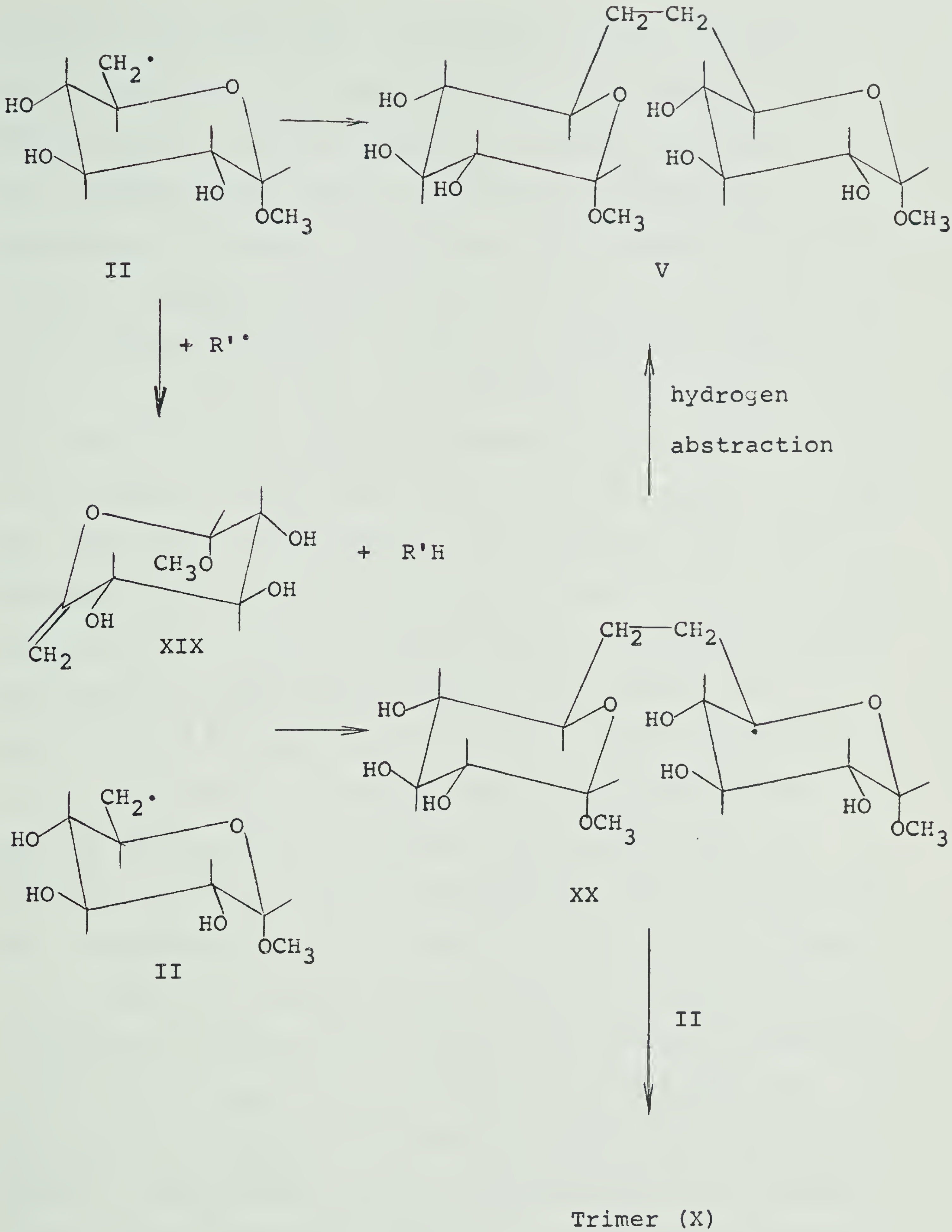
incorporated at carbon-6 be obtained. Comparison of the mass spectrum of XVII with that of the non-deuterated compound, methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside, IV, measured under identical conditions suggested that 1.5% of XVII contained a deuterium atom at carbon-6. Since the primary kinetic isotope effect for hydrogen abstraction varies from 1 to 8 (48) the quantity of methyl 6-deoxy-α-D-glucopyranoside formed due to the abstraction of a hydrogen from carbon-1 would be in the range 1.5 to 12% depending on the actual primary kinetic isotope effect in this case.

The dimer, XVI, obtained in 9.3% yield from the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d was acetylated to give methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-glucopyranoside-1-d]-6-yl)-α-D-glucopyranoside-1-d hexaacetate, XVIII. The p.m.r. spectrum of XVIII in deuteriochloroform (Fig. 19) showed the chemical shifts listed in Table VIII. As would be expected the chemical shifts of the ring protons are similar to those obtained for methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranoside-1-d, XVII. Irradiating the dimer, XVIII, at 6.22τ (H_5) caused the multiplet at 8.25 - 8.4τ ($H_{6,6'}$) to collapse to a singlet.

When a 12 x 10^{-2} M solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside was photolysed the yield of the 6-deoxy compound, III, was 23% and the yield of the dimer, V, was 5.8%; however, photolysis of a 2.85 x 10^{-2} M solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d gave a 15.6%

yield of the 6-deoxy compound and a 9.3% yield of dimer, XVI. In order to show that this change in yield was due to the change in concentration and not to a kinetic isotope effect a 2.85×10^{-2} M solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside was photolysed. Isolation of the products gave a 15.3% yield of the 6-deoxy compound III, and a 10.4% yield of the dimer, V. These results show that, within experimental error, the yield of the 6-deoxy compound, III, and the dimer, V, are the same with or without deuterium at carbon-1. It is apparent that the percentage yield of III decreases and the percentage yield of the dimer, V, increases, with decreasing concentration of starting material.

Two mechanisms are readily envisaged for the formation of the dimer, V. Obviously, the straightforward coupling of two primary radicals is indicated. However, as was mentioned in the Introduction, the photolysis of alkyl iodides is well known to yield alkenes. It would be expected that the methyl 6-deoxy-α-D-glucopyranoside radical, II, formed by the loss of an iodine atom by the 6-iodo compound, I, would disproportionate either with a second methyl 6-deoxy-α-D-glucopyranoside radical or with an iodine atom, to form methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside, XIX. The other product would be either methyl 6-deoxy-α-D-glucopyranoside, III, or hydrogen iodide depending on whether the radical II disproportionated with another radical (II) or with an iodine atom. As discussed in the Introduction, previous work on the photolysis of alkyl iodides (9 - 13) was done using organic



II
V
+ R'•
hydrogen abstraction
XIX
+ R'H
XX
II
II
Trimer (X)

solvents. This meant that the hydrogen iodide, formed by disproportionation, was available as a good source of hydrogen atoms. In this research the solvent used was water, buffered with sodium bicarbonate, which would immediately neutralise any hydrogen iodide formed. Methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside, XIX, must be expected to be a highly efficient scavenger for radicals, especially since it is a vinyl ether, and therefore, the formation of the dimeric radical, XX, must be expected. The further reaction of the dimeric radical, XX, with either the radical II or the enol ether, XIX, could explain the formation of the higher molecular weight products (trimers) obtained in each case from the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside. The formation of the dimeric radical, XX, suggests the possibility of inversion at the radical centre (carbon-5) to give the methyl β-L-idopyranoside configuration after hydrogen abstraction. No compound was isolated from the photolysis mixture, with the spectroscopic data expected for such a compound. This is in accord with the work of Lehmann (2) who added the toluene-α-thiol radical to methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside to give only methyl 6-S-benzyl-6-thio-α-D-glucopyranoside. As mentioned previously the hydrogen-atom acceptor R' in the formation of XIX could be either an iodine atom or another radical such as II formed in the initial photolysis reaction. It would be of interest to photolyse methyl 6-deoxy-6-iodo-α-D-glucopyranoside-5-d

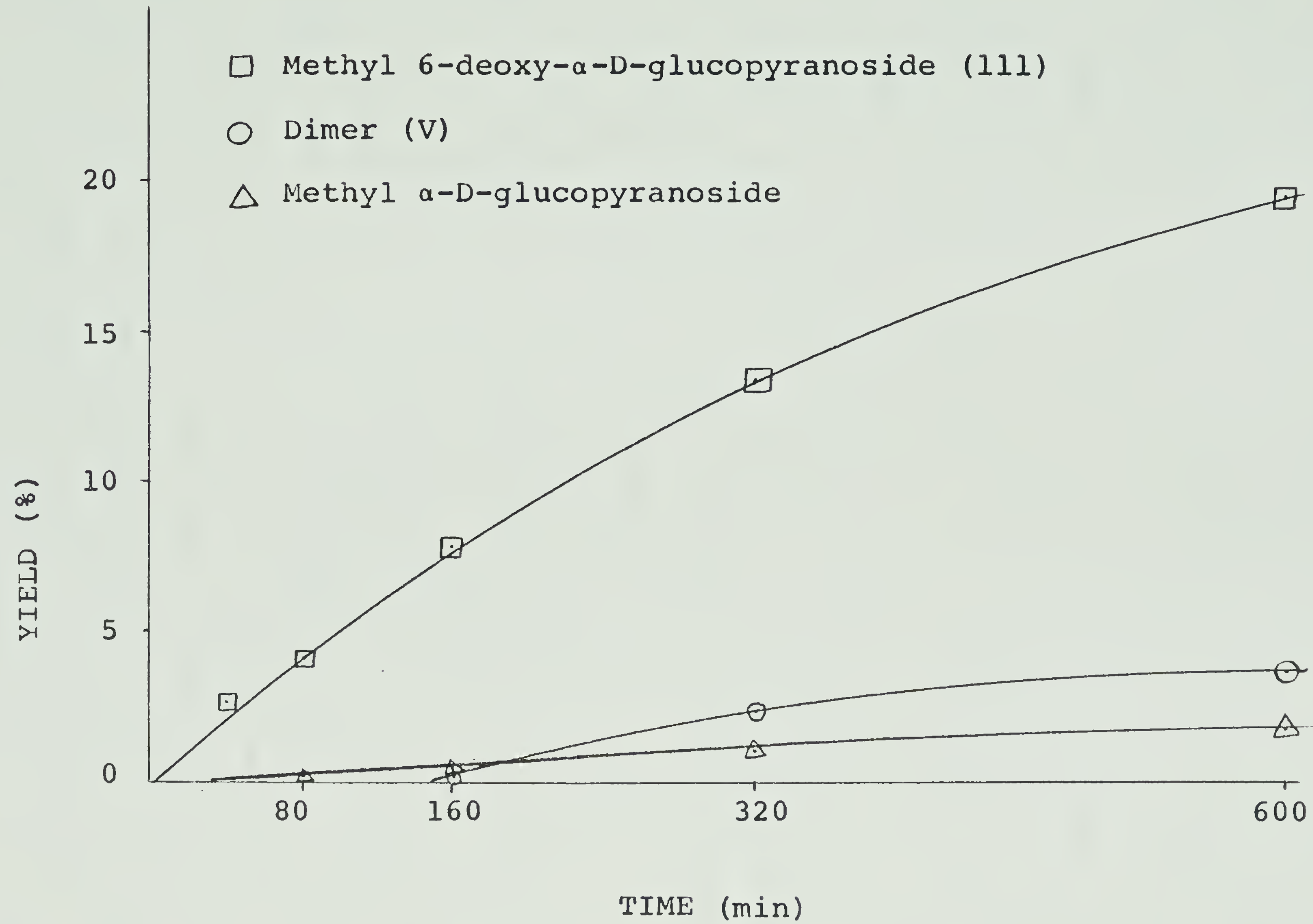


FIG. 22. Products from the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside as analysed by g.l.c. (trimethylsilyl derivative)

to see whether or not 5,6-dideuterated methyl 6-deoxy-α-D-glucopyranoside would form.

An attempt was now made to follow the rate of formation of methyl 6-deoxy-α-D-glucopyranoside III, methyl α-D-glucopyranoside, and dimer V, by photolysing a 0.12 M solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, buffered with sodium bicarbonate. Aliquots were removed at the intervals shown in Table III and, after the addition of a known quantity of pentaerythritol to each aliquot, they were treated with sodium hydroxide, deionised with ion-exchange resin, and the trimethylsilyl derivative of each aliquot was prepared. Gas-liquid chromatographic analysis of each aliquot gave the results shown graphically in Fig. 22. The results obtained after ten hr photolysis: methyl 6-deoxy-α-D-glucopyranoside (III), yield 20%; methyl α-D-glucopyranoside, yield 1.7%; and dimer (V), yield 3.6%, are in good agreement with the results obtained by preparative chromatography since no allowance is made for the reaction not going to completion. Two points of interest are apparent from an examination of the results. It is apparent that the methyl α-D-glucopyranoside is a product of the photolysis reaction and is not merely the result of solvolysis of the iodide by the basic solution. This is shown by the fact that the unphotolysed aliquot, which was allowed to stand for the same period as each of the photolysed samples, contained no methyl α-D-glucopyranoside. The other

interesting feature of the results is that apparently for approximately the first one hundred and fifty minutes of the photolysis reaction no dimer (V) is formed. This induction period suggests that the formation of dimer (V) requires a build up of the concentration of some intermediate compound such as the enol ether, XIX. It was not possible to say from the gas-liquid chromatographic results whether or not a small quantity of methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside, XIX, was formed in the reaction, since the trimethylsilyl derivative of XIX showed exactly the same retention time as the trimethylsilyl derivative of the 6-deoxy compound, III.

Although no methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside, XIX, had been isolated or detected chromatographically in the reaction mixture it was decided to investigate the effect on the reaction of adding additional XIX. A solution, 0.03 molar in methyl 6-deoxy-6-iodo-α-D-glucopyranoside, I, 0.06 molar in methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside, XIX, buffered with sodium bicarbonate was photolysed for four hours. Isolation of the products by Celite column chromatography gave: methyl 6-deoxy-α-D-glucopyranoside, III, yield 15.2%; methyl α-D-glucopyranoside, yield 3.3%; dimer, V, yield 9.0%; together with unchanged methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside, 53% recovered. Finally, elution of the Celite column with water gave, after removal of cations with Amberlite IR 120 H^+ resin, a brown residue (926 mg) whose p.m.r. spectrum was similar to the p.m.r. spectrum of compound X (polymer), obtained when the photolysis was done in the

absence of added XIX. This brown residue (926 mg) is equal to ~83% of the weight of methyl 6-deoxy-6-iodo-α-D-glucopyranoside photolysed when allowance is made for the loss of the iodine atom. However, in the presence of added XIX the yield of X is approximately three times greater than in the absence of XIX. This increase in the yield of polymer supports the mechanism postulated earlier for its formation; addition of a radical, such as the methyl 6-deoxy-α-D-glucopyranoside radical, II, to methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside, XIX, to give the dimer radical, XX, which could react either with a further molecule of the enol ether, XIX, or couple with some other radical to complete the chain. The yield of the dimer, V, is relatively little changed by the addition of the enol ether, XIX, to the photolysis reaction. To show that the increase in the yield of polymer was not due merely to the interaction of the enol ether, XIX, with the ultraviolet light, a solution of methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside, XIX, buffered with sodium bicarbonate was photolysed. Examination of the p.m.r. spectrum of the residue, after concentration, showed that the residue consisted of virtually unchanged methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside.

The dissociation energy of the carbon-iodine bond in methyl 6-deoxy-6-iodo-α-D-glucopyranoside is considered to be 50 - 55 kcal/mole (49) by analogy with the results obtained for simple alkyl iodides. In view of the energy of

the ultraviolet light used (2537 Å, 113 kcal/mole) each mole of methyl 6-deoxy-6-iodo-α-D-glucopyranoside which absorbed a photon of energy and dissociated into a methyl 6-deoxy-α-D-glucopyranoside radical and an iodine atom would be left with approximately 63 kcal (113 - 50) of excess energy. This energy would be present in the form of kinetic energy and in the case of the methyl 6-deoxy-α-D-glucopyranoside radical, it would be present as translational and rotational energy. Since a "hot" methyl 6-deoxy-α-D-glucopyranoside radical would rapidly dissipate its excess of translational and rotational energy to the solvent water molecules the only carbon-hydrogen bond with a lower dissociation energy than the corresponding carbon-hydrogen bond in methyl α-D-glucopyranoside would be at carbon-5. This is because the hydrogen beta to a radical has a lowered bond dissociation energy. The abstraction of such a beta hydrogen by a radical is known as disproportionation and, as was discussed previously this is a possible source of portion of the 6-deoxy compound, III. Normally with primary radicals the number of radicals undergoing disproportionation is a small fraction of the number undergoing combination depending on the number of beta hydrogens available. In view of the relatively small yield of dimer V, obtained in the reaction it seems likely that little if any of the methyl 6-deoxy-α-D-glucopyranoside, III, is formed by disproportionation.

An aqueous 6 x 10^{-2} M solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, buffered with sodium bicarbonate, was photolysed in the presence of a two molar ratio of methyl α-D-glucopyranoside. It was considered that if the radical, formed by the loss of an iodine atom from methyl 6-deoxy-6-iodo-α-D-glucopyranoside, was abstracting a hydrogen from positions, 1, 2, 3, 4 or 5 in another molecule of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, it would abstract a hydrogen from the same position of methyl α-D-glucopyranoside. If this was the case it was expected that the yield of methyl 6-deoxy-α-D-glucopyranoside would be increased. The products from the photolysis reaction were separated by chromatography on a carbon-Celite column using gradient elution with ethanol-water. By eluting the column initially with water it was possible to elute the excess methyl α-D-glucopyranoside from the column before the reaction products were eluted from the column. Collection of appropriate fractions followed by deionising with ion-exchange resins gave methyl 6-deoxy-α-D-glucopyranoside, III, in 22% yield and dimer, V, in 7% yield. These yields are approximately the yields that would have been predicted, on the basis of previous work, for the photolysis of a 6 x 10^{-2} M solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside without methyl α-D-glucopyranoside. This result suggests that the source of hydrogen-atoms is largely either carbon-6 of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, I, or degradation products formed by the photolysis of I.

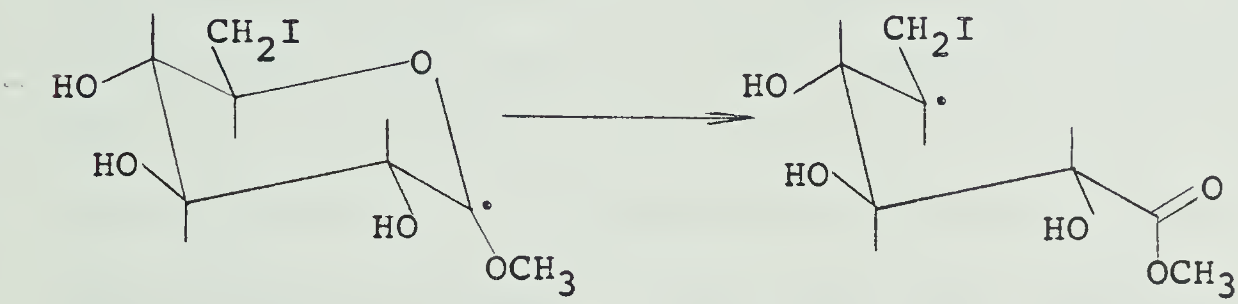
If the methyl 6-deoxy-α-D-glucopyranoside radical, II, abstracts a hydrogen atom from a carbon atom carrying a secondary hydroxyl group it is possible that the resulting radical would react with an iodine atom to form an α-halo alcohol which would be expected to eliminate hydrogen iodide leaving a ketone.

$$\mathrm{HO{-}\overset{|}{\underset{|}{C}}{-}H} + \mathrm{R\cdot} \longrightarrow \mathrm{HO{-}\overset{|}{\underset{|}{C}}\cdot} + \mathrm{RH} \xrightarrow{\mathrm{I\cdot}} \mathrm{HO{-}\overset{|}{\underset{|}{C}}{-}I} \longrightarrow \mathrm{\overset{|}{\underset{|}{C}}{=}O} + \mathrm{HI}$$

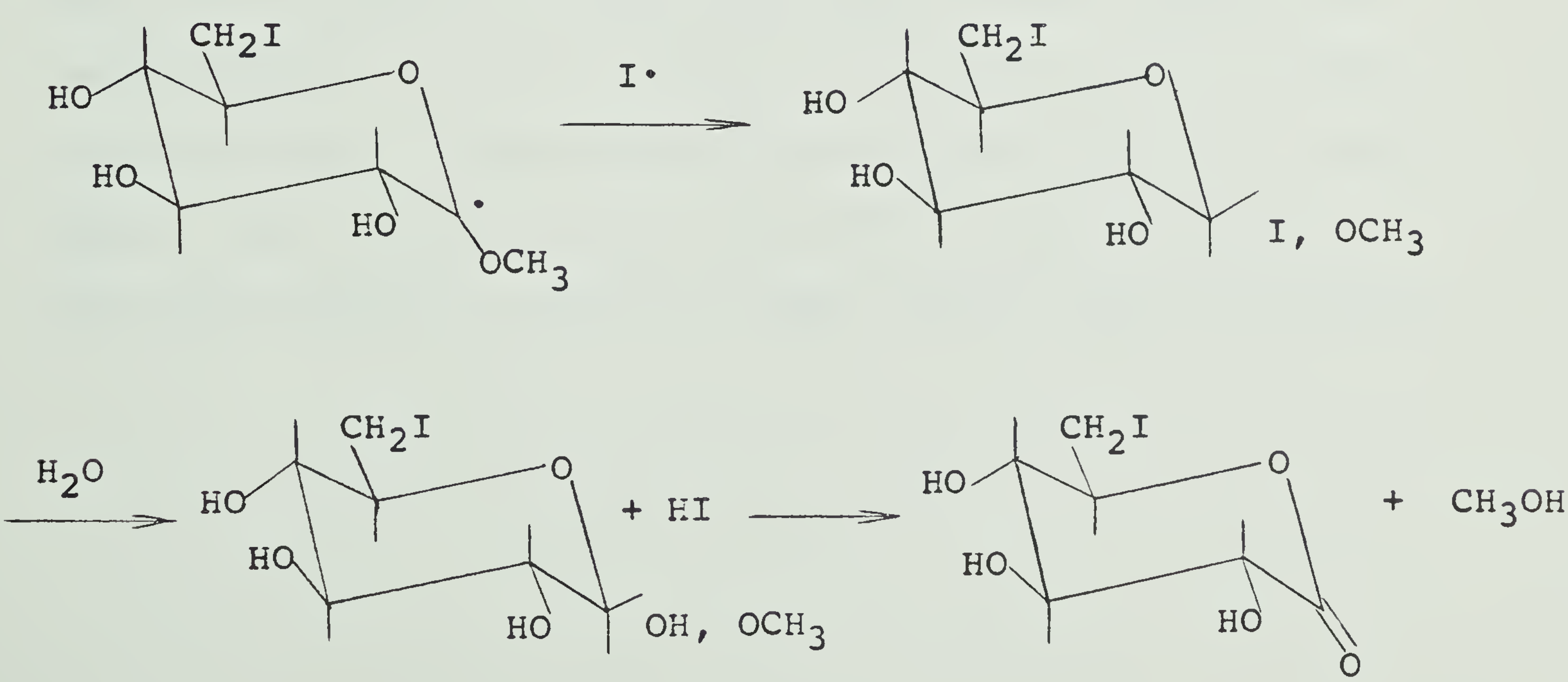
This mechanism is similar to the mechanism proposed by Kharasch and Friedman (13) to explain the oxidation of methanol to formaldehyde when iodoaromatic compounds were photolysed in methanol. A mechanism of this type would also explain the reduction of iodine atoms to iodide ions with the production of one mole of acid. However, this mechanism does not demonstrate how approximately 1.3 moles of acid could be produced for each mole of methyl 6-deoxy-6-iodo-α-D-glucopyranoside which is photolysed.

Investigation by mass spectroscopy of the acetate of methyl 6-deoxy-α-D-glucopyranoside-1-d obtained from the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d, as described earlier, showed that up to a maximum of approximately 12% of the methyl 6-deoxy-α-D-glucopyranoside produced was formed by the abstraction of the anomeric

hydrogen at carbon-1. The radical formed in this way could react with an iodine atom before it underwent a β-scission reaction of the type demonstrated by Huyser (50) for the reaction of 2-methoxy tetrahydropyran with di-t-butyl peroxide to give methyl valerate.

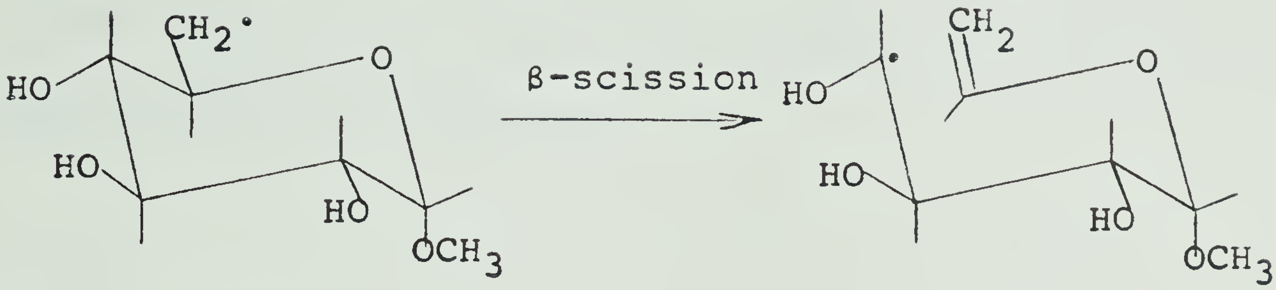


Elimination of hydrogen iodide by the compound formed by the addition of an iodine atom to the free radical at carbon-1 would yield the δ-lactone.



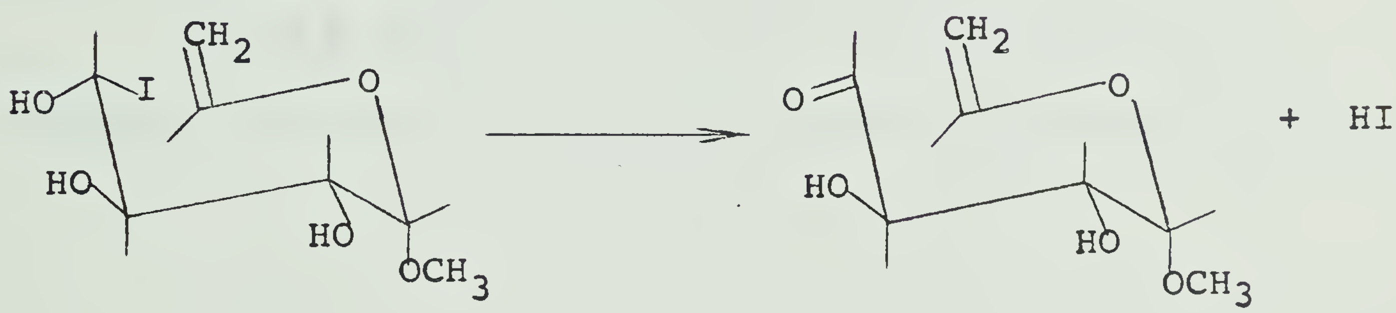
This mechanism is attractive in that it involves the reduction of an iodine atom to an iodide ion with the production of methanol, together with the possibility of the δ-lactone reacting with sodium bicarbonate to neutralise a total of two moles of sodium bicarbonate for each mole of starting material which reacts in this way. That this reaction takes place to only a small extent has been shown by both the experiments with the 1-deutero compound and by the fact that adding a two mole excess of methyl α-D-glucopyranoside to a solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside before it was photolysed resulted in little apparent increase in the yield of methyl 6-deoxy-α-D-glucopyranoside.

A further possible reaction route for the methyl 6-deoxy-α-D-glucopyranoside radical, II, would be via a β-scission reaction (51) in which the pair of electrons beta to the radical is split to form an olefine and another radical. When it is possible to form more than one new radical the radical formed is the one which is the most stable. In the case of methyl 6-deoxy-α-D-glucopyranoside radical it would appear that the most stable new radical would be the one with the radical at carbon-4 rather than on the ring oxygen.



II

A possible mode of reaction of the new radical would be combination with an iodine atom followed by elimination of hydrogen iodide to give an aldehyde.



The source of iodine could be a free iodine atom, a molecule of iodine, or a compound such as methyl 6-deoxy-6-iodo-α-D-glucopyranoside which contains an iodine atom. An aldehyde group, formed in this manner, would be a source of hydrogen atoms for other radicals formed in the reaction. Abstraction

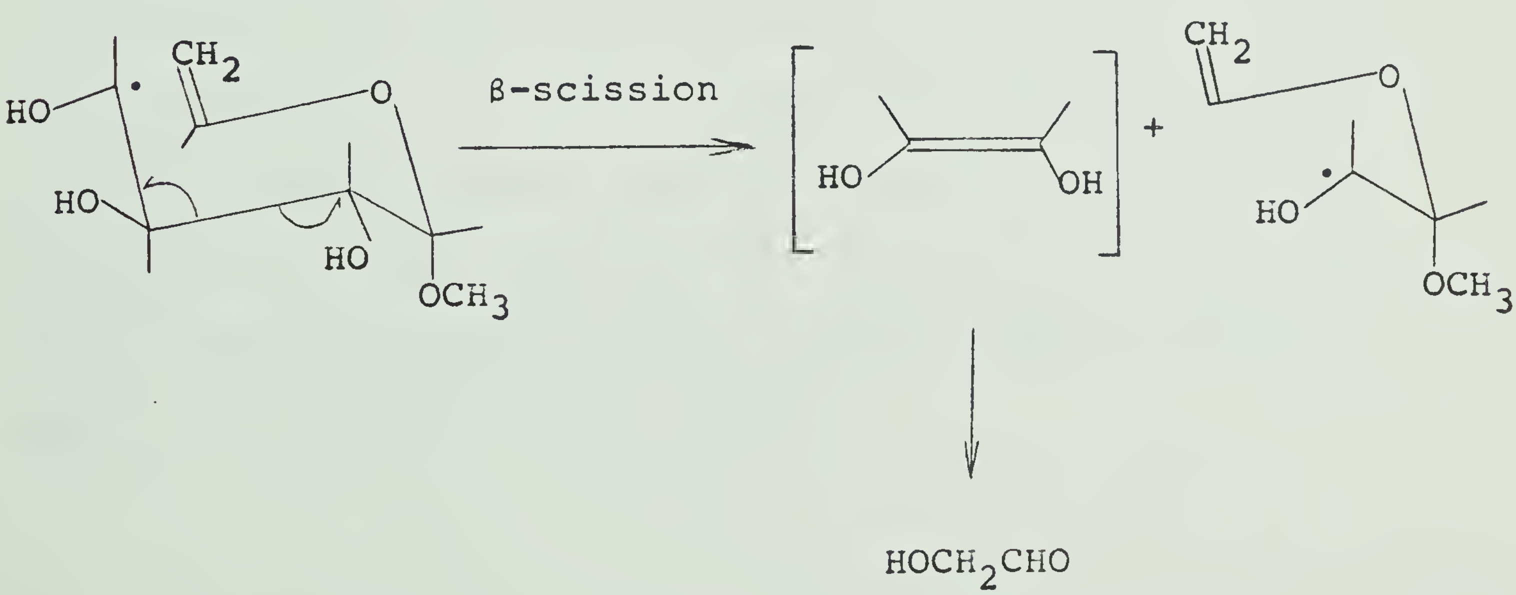
of the hydrogen atom from the aldehyde, followed by reaction with an iodine atom and solvolysis with water would result in the formation of two moles of acid for each mole of aldehyde which reacted in this way.

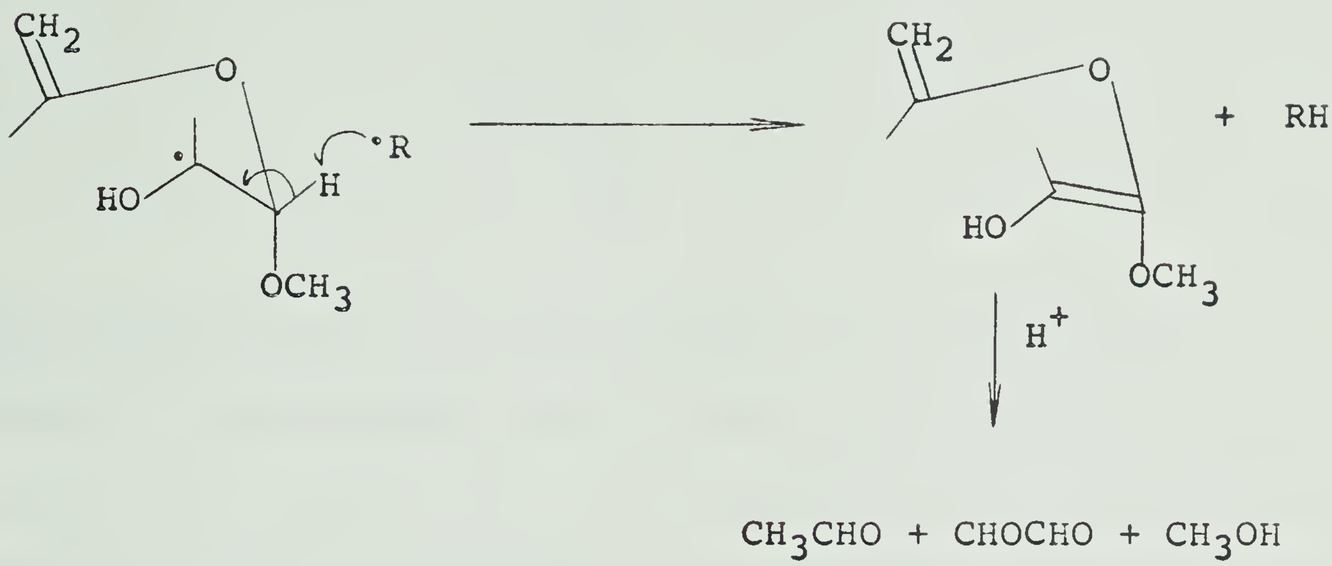
$$\mathrm{R{-}\overset{\overset{H}{|}}{C}{=}O} + \mathrm{R'\cdot} \longrightarrow \mathrm{R'H} + \mathrm{R{-}\dot{C}{=}O} \xrightarrow{\mathrm{I\cdot}} \mathrm{R{-}\overset{\overset{I}{|}}{C}{=}O}$$

$$\mathrm{R{-}\overset{\overset{I}{|}}{C}{=}O} + \mathrm{H_2O} \longrightarrow \mathrm{R{-}\overset{\overset{OH}{|}}{C}{=}O} + \mathrm{HI}$$

Radicals formed during the photolysis reaction would be expected to add to the olefine produced by β-scission of the methyl 6-deoxy-α-D-glucopyranoside radical.

On the other hand the new radical formed by a β-scission reaction could undergo further β-scission reactions.





It was not found possible to estimate the amount, if any, of the methyl 6-deoxy-α-D-glucopyranoside radical undergoing β-scission.

The foregoing results have shown that indeed the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside produced the primary radical, II. This radical when formed in aqueous solution appeared to show considerable stability in view of the rather high yield of methyl 6-deoxy-α-D-glucopyranoside, III, (about 23%) formed when the only source of hydrogen atoms was either starting material or products of its photolysis. In order to test this hypothesis it was decided to carry out the photolysis in the presence of an abundance of a good hydrogen-atom donor. Acetaldehyde was chosen for this purpose since in aqueous media it should readily be converted to the radical:

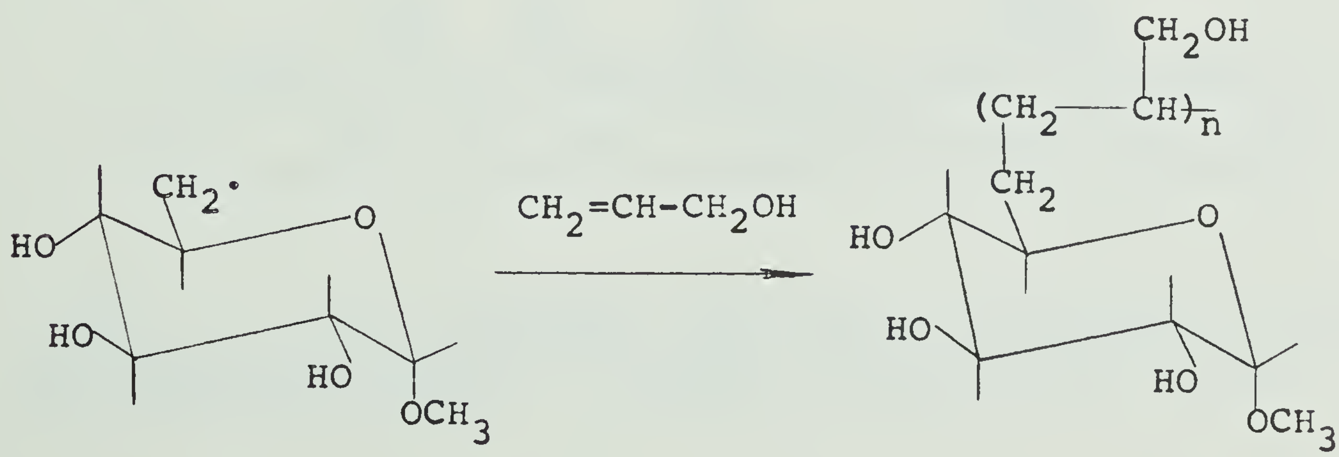
$$CH_3-\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle OH}{|}}{C}}\cdot$$

The photolysis of I in the presence of a fifty molar excess of acetaldehyde gave an 80% yield of methyl 6-deoxy-α-D-glucopyranoside, III. This experiment clearly shows that these photolyses can indeed be of synthetic value when carried out in the presence of a suitably reactive radical acceptor. In order to demonstrate this fact, it was decided to carry out the reaction in the presence of an alkene (allyl alcohol) and in the presence of formaldehyde which is known (52) to add radicals to form, eventually, a carbinol.

$$R\cdot \quad + \quad CH_2O \longrightarrow RCH_2OH$$

The addition of a radical to an olefine is well known to be usually an energetically favourable reaction with a low activation energy (53). The radical thus produced can be expected to attack a second molecule of the olefine and thus initiate a polymerization reaction which can be terminated only by a hydrogen-atom donor or by coupling with another radical. When a solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, buffered with sodium bicarbonate,

was photolysed in the presence of a fifty molar excess of redistilled allyl alcohol it was apparent from the increased weight of the residue that polymerization had occurred. Also, it was apparent from the p.m.r. spectrum (Fig. 23) of the residue that the yield of methyl 6-deoxy-α-D-glucopyranoside was less than the yield obtained when methyl 6-deoxy-6-iodo-α-D-glucopyranoside was photolysed in the absence of allyl alcohol. An attempt was made to separate the residue according to its degree of polymerisation, by chromatographing it on a column of medium Sephadex G25. Although a complete separation was not achieved, the experiment was partially successful in that when the fractions obtained were investigated by measuring their specific rotation and p.m.r. spectra it was apparent that the higher polymers were eluted from the Sephadex column before the lower polymers. Calculations based on the p.m.r. spectrum, specific rotation and molecular weight of the first fraction eluted from the column suggested that the largest polymers contained 10 - 20 molecules of allyl alcohol for each molecule of methyl 6-deoxy-α-D-glucopyranoside.



II

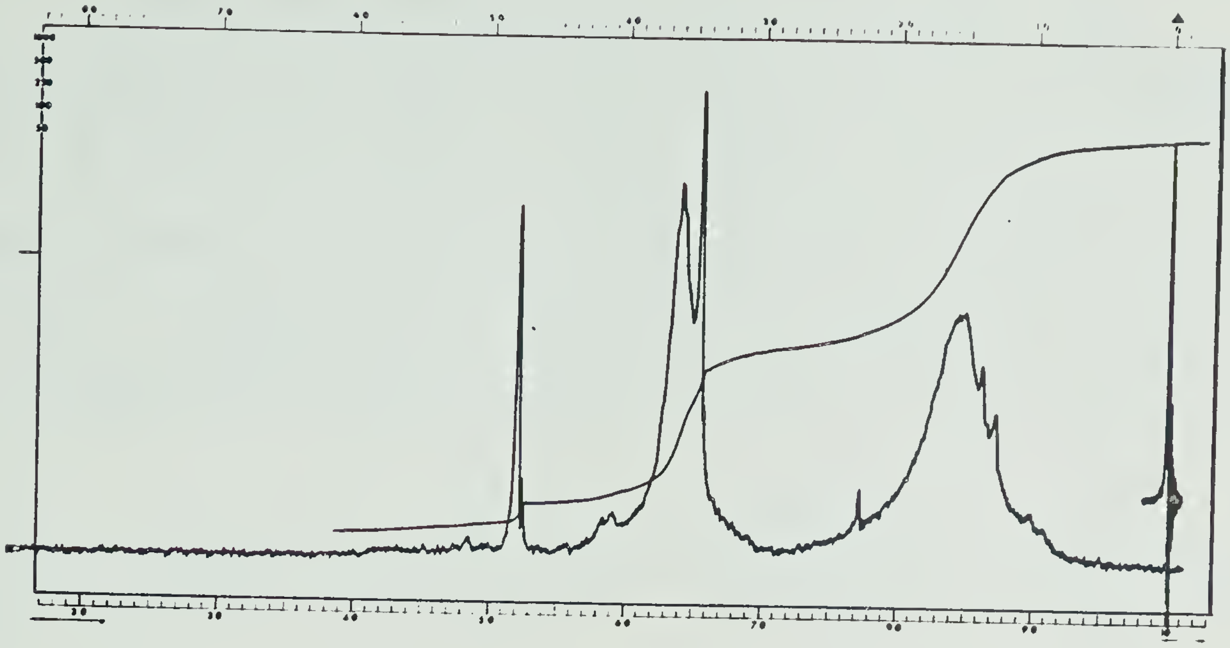


FIG. 23. P.m.r. spectrum (60 Mc.p.s.) of product from the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside in the presence of allyl alcohol. (deuterium oxide)

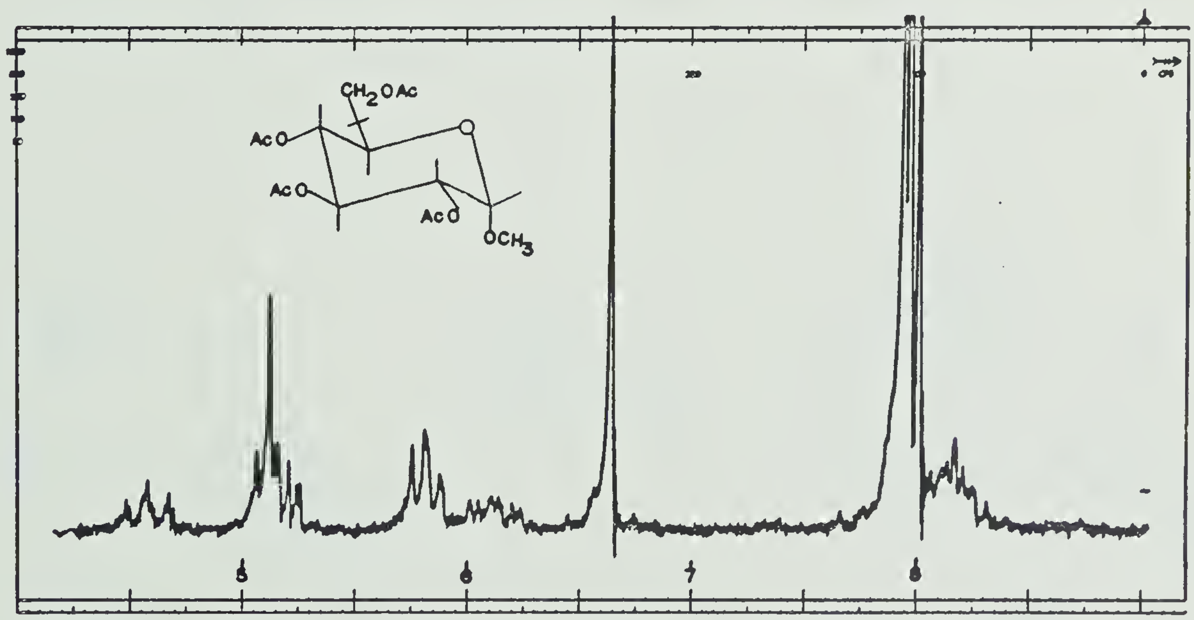
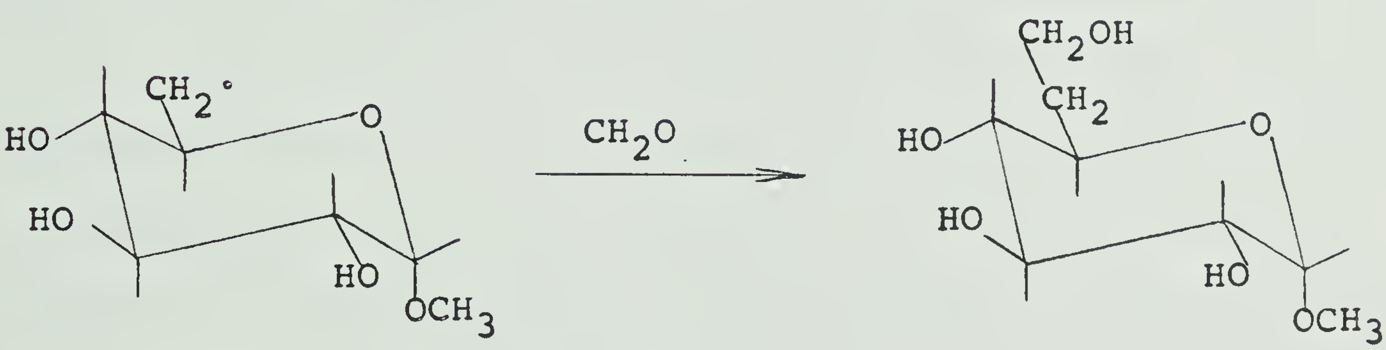


FIG. 24. P.m.r. spectrum (100 Mc.p.s.) of methyl 2,3,4,7-tetra-O-acetyl-6-deoxy-α-D-gluco-heptopyranoside (XXII) (deuteriochloroform)

Rust and coworkers (52, 54) have shown that alkyl radicals will add to the carbon atom of an aldehyde group to give an alcohol, after hydrogen abstraction by the oxygen radical. Minoru Oyama (55) has investigated a similar addition of hydroxyalkyl radicals to formaldehyde which also appears to involve addition to the carbonyl group.

$$\mathrm{HO{-}\overset{\displaystyle R}{\underset{\displaystyle R}{\overset{|}{\underset{|}{C}}}}\cdot} + \mathrm{CH_2O} \longrightarrow \mathrm{HO{-}\overset{\displaystyle R}{\underset{\displaystyle R}{\overset{|}{\underset{|}{C}}}}{-}CH_2{-}O\cdot} \xrightarrow[\text{abstraction}]{\text{hydrogen}} \mathrm{HO{-}\overset{\displaystyle R}{\underset{\displaystyle R}{\overset{|}{\underset{|}{C}}}}{-}CH_2OH}$$

It was decided therefore to test the possibility of preparing methyl 6-deoxy-α-D-gluco heptopyranoside, XXI, by adding the radical, II, formed by the photolysis of the iodide, I, to formaldehyde.



II XXI

An aqueous solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, buffered with sodium bicarbonate, was photolysed in the presence of an eleven molar excess of formaldehyde for ten hours. Titration of aliquots removed from the solution before and after it was photolysed showed that 1.3 moles of sodium bicarbonate were neutralised for each mole of methyl 6-deoxy-6-iodo-α-glucopyranoside initially present. Examination of the reaction product by t.l.c. indicated the presence of a compound not observed when the solution was photolysed in the absence of formaldehyde.

The photolysis reaction was repeated using similar quantities of reagents. After irradiation for eight and one half hours the solution was concentrated *in vacuo* and the paraformaldehyde removed by repeatedly adding water and concentrating *in vacuo*. The residue was separated by n-butanol-water partition chromatography on a Celite column. Investigation of the first fraction eluted from the column showed it to be unchanged methyl 6-deoxy-6-iodo-α-D-glucopyranoside (14.5% was recovered). The second fraction was shown to be methyl 6-deoxy-α-D-glucopyranoside and represented a 25.5% yield of the unrecovered methyl 6-deoxy-6-iodo-α-D-glucopyranoside. In order to purify the third fraction it was necessary to acetylate the mixture before separating it on a silicic acid column eluted with chloroform. Concentration of the major

fraction gave a 6.8% yield of a syrup, XXII, which crystallised from ethanol-water and whose structure was shown indeed to be methyl 2,3,4,7-tetra-O-acetyl-6-deoxy-α-D-gluco-heptopyranoside, XXII. The p.m.r. spectrum of XXII (Fig. 24) measured in deuteriochloroform showed protons with the following chemical shifts (τ value): H_1, H_2, H_4, 5.0 - 5.25 (3H); H_3, 4.56 (broad triplet, 1H); H_5, 6.12 (sextet, 1H); $H_{6,6'}$, 8.0 - 8.25 (multiplet, 2H); $H_{7,7'}$, 5.8 (broad triplet, 2H); methoxyl, 6.66 (3H); four acetyl, 7.9 - 8.04 (12H). Irradiation of the sample at 8.14τ showed these protons, $H_{6,6'}$ to be coupled to the sextet at 6.12τ (H_5) and to the broad triplet at 5.8τ ($H_{7,7'}$). These results, together with the results of an elemental analysis and a molecular weight determination were interpreted in terms of the structure methyl 2,3,4,7-tetra-O-acetyl-6-deoxy-α-D-gluco-heptopyranoside for XXII. This structure was confirmed by degradative studies (see below) on the deacetylated glycoside (XXI).

Remaining fractions eluted from the Celite column were acetylated and separated on silicic acid columns eluted with chloroform. The only compound identified was methyl 2,3,4,6-tetra-O-acetyl-α-D-glucopyranoside which was obtained in a 1.3% yield. It was not found possible to isolate any of the dimer, V.

The photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside was repeated in the presence of a 22.4 molar excess of formaldehyde. After concentration *in vacuo* the

paraformaldehyde was removed as described previously and the residue separated by n-butanol-water partition chromatography on a Celite column. The following fractions were collected: methyl 6-deoxy-6-iodo-α-D-glucopyranoside (9.6% was recovered); methyl 6-deoxy-α-D-glucopyranoside, III, yield 33.8%; methyl 6-deoxy-α-D-*gluco*-heptopyranoside, XXI, yield 10%; methyl α-D-glucopyranoside, yield 3.8%. In this case the methyl 6-deoxy-α-D-*gluco*-heptopyranoside, XXI, was purified by passing it through ion-exchange resins.

The p.m.r. spectrum of methyl 6-deoxy-α-D-*gluco*-heptopyranoside (Fig. 25) measured in deuteriopyridine showed protons with the following chemical shifts (τ value): H_1, 4.96 (doublet, 1H); H_2, 5.96 (quartet); H_3, 5.58 (triplet, 1H); H_4, 6.23 (triplet, 1H); H_5, $H_{7,7'}$, 5.6 - 6.0; H_6, ~7.25 (multiplet); $H_{6'}$, ~7.9 (multiplet); methoxyl, 6.59 (singlet, 3H). Coupling constants (c.p.s.) were: $J_{1,2}$, 3.5; $J_{2,3}$, 9.0; $J_{3,4}$, 9.0; $J_{4,5}$, 9.0. Irradiation of the sample at 5.85τ caused the collapse of the $H_{6,6'}$ signals, 7.1 - 8.1τ, as shown in Fig. 25. As would be expected for two methylene protons adjacent to an assymmetric centre the $H_{6,6'}$ multiplets appear to collapse to an AB pattern (56). A comparison of the chemical shifts and coupling constants assigned to the ring protons of methyl 6-deoxy-α-D-*gluco*-heptopyranoside, XXI, with the chemical shifts and coupling constants of the ring protons of the known methyl 6-deoxy-α-D-glucopyranoside, III, shown in Table IX confirms the assignment of an α-D-gluco-pyranoside configuration to XXI.

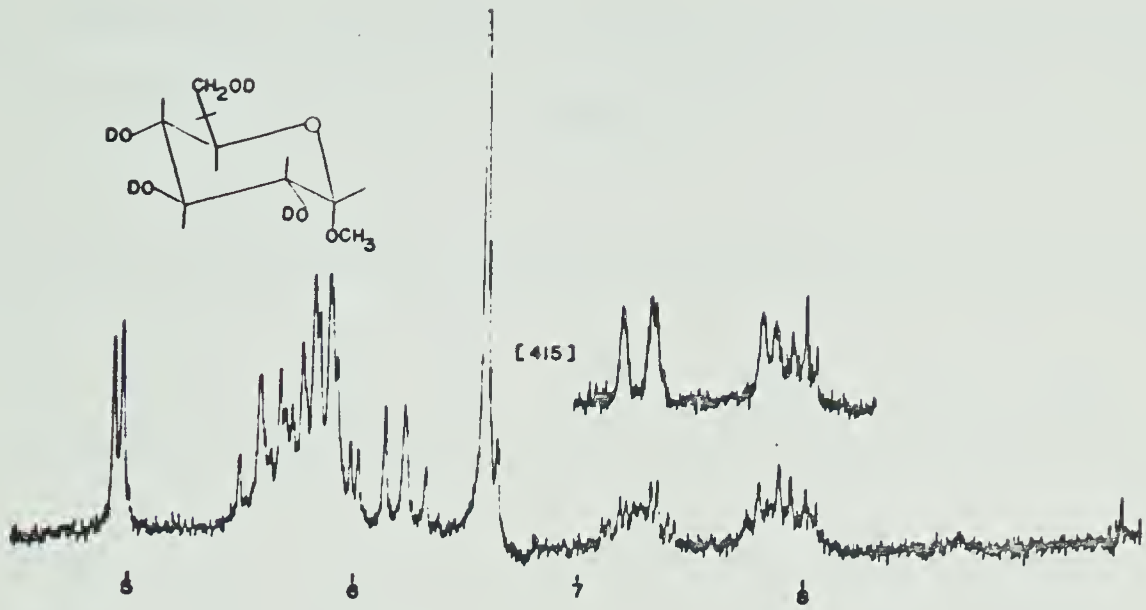


FIG. 25. P.m.r. spectrum (100 Mc.p.s.) of methyl 6-deoxy-α-D-gluco-heptopyranoside (XXI) (deuteriopyridine)

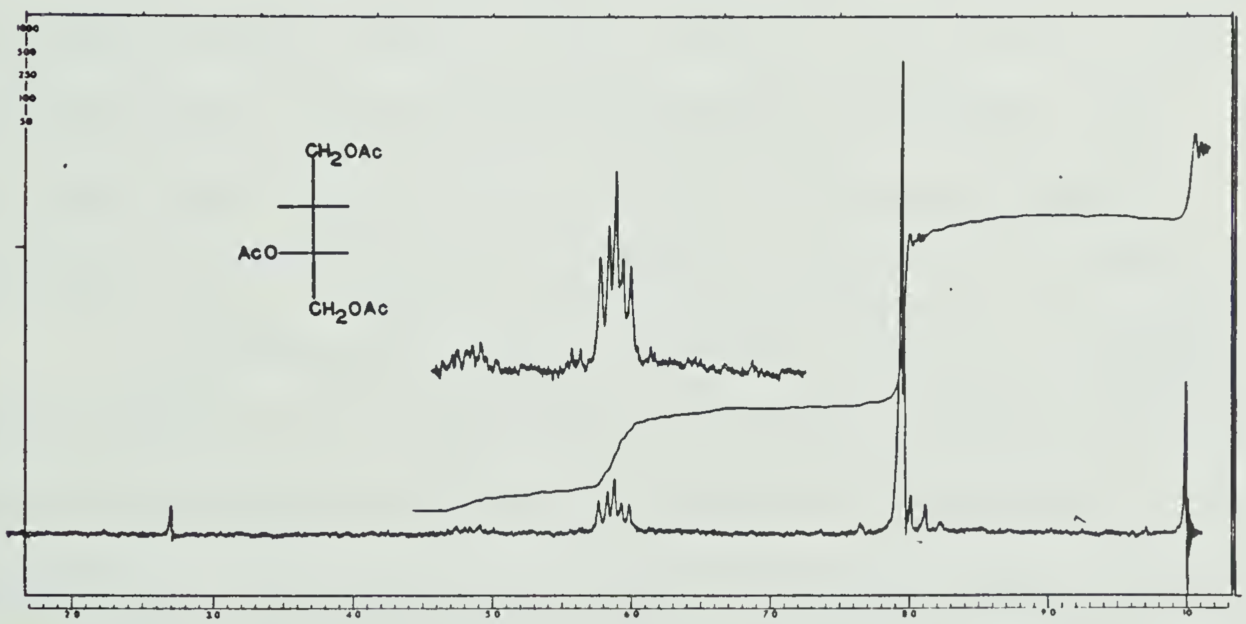


FIG. 26. P.m.r. spectrum (60 Mc.p.s.) of 1,2,4-butanetriol triacetate (XXIV) (deuteriochloroform)

TABLE IX

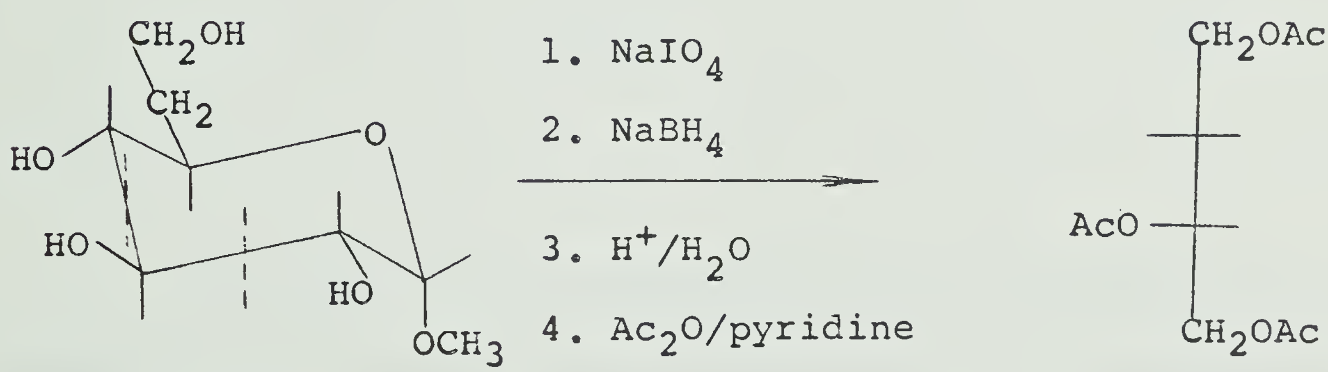
P.M.R. Parameters for Methyl 6-deoxy-α-D-glucopyranoside, III, and Methyl 6-deoxy-α-D-*gluco*-heptopyranoside, XXI.

	H_1	H_2	H_3	H_4	H_5	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
III	5.08	6.05	5.70	6.46	6.00	3.5	9.5	8.5	9.5
XXI	4.96	5.96	5.58	6.23	--	3.5	9.0	9.0	9.0

A sample of methyl 6-deoxy-α-D-*gluco*-heptopyranoside was reacted with excess sodium periodate using the conditions described by Guthrie (57) to determine the number of vicinal hydroxyl groups. Aliquots were removed at intervals and titrated using the Mueller-Friedberger technique (36). It was found that each mole of methyl 6-deoxy-α-D-*gluco*-heptopyranoside consumed two moles of sodium periodate.

A further quantity of methyl 6-deoxy-α-D-*gluco*-heptopyranoside was oxidized with excess sodium periodate and the resulting aldehyde groups were reduced with sodium borohydride. The aqueous product was heated with Amberlite IR 120 (H^+) resin to hydrolyse the acetal linkage. Concentration *in vacuo* gave a syrup, XXIII, which was shown by paper chromatography and by comparison of p.m.r. spectra to be indistinguishable from an authentic sample of 1,2,4-butanetriol.

Acetylation of XXIII gave a syrup, XXIV, whose p.m.r. spectrum (Fig. 26) and I.R. spectrum were identical to the spectra obtained for authentic 1,2,4-butanetriol triacetate. Both individually and when mixed compound XXIV showed the same retention time as 1,2,4-butanetriol triacetate when the two were subjected to gas-liquid chromatography. On the basis of the structure, methyl 6-deoxy-α-D-*gluco*-heptopyranoside, assigned to XXI the stereochemistry of XXIV must be 1,2,4-tri-*O*-acetyl-3-deoxy-D-*glycero*-tetritol. The isolation of this 3-deoxy-tetritol confirms the structure methyl 6-deoxy-α-D-*gluco*-heptopyranoside which had been assigned to XXI on the basis of its p.m.r. spectrum.

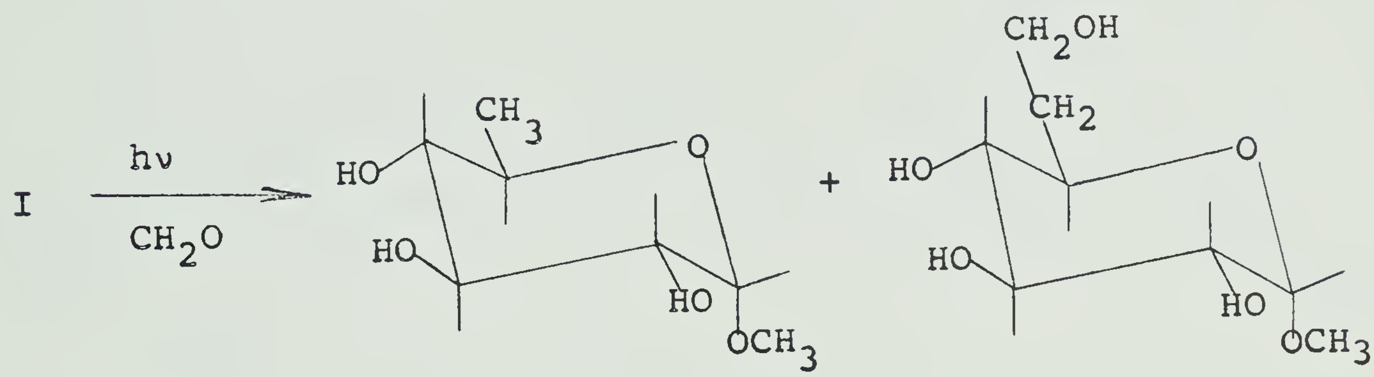


XXI

XXIV

The photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside was repeated in the presence of a one hundred molar excess of formaldehyde. Separation of the reaction products as before gave a 42% yield of methyl 6-deoxy-α-D-

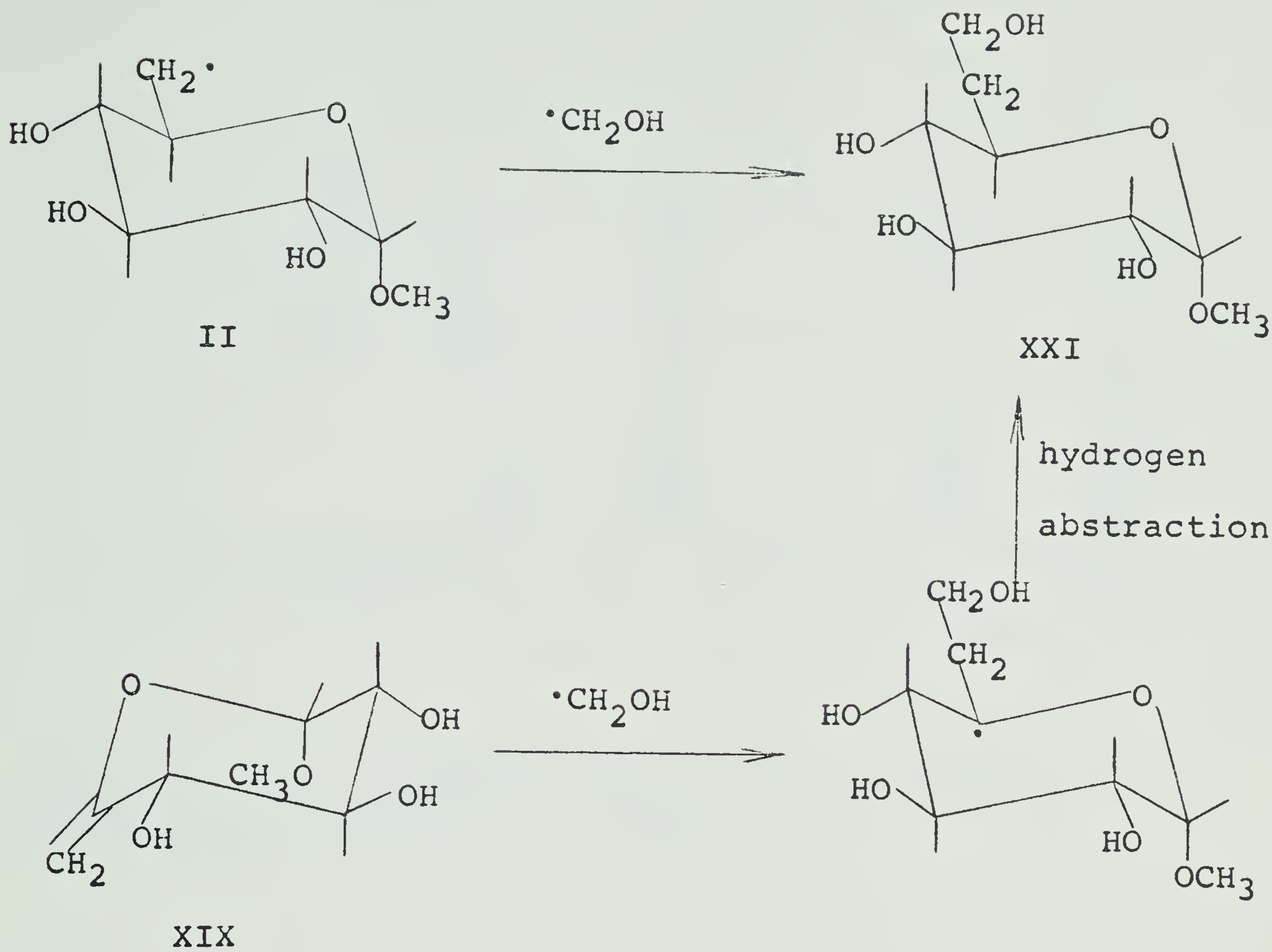
glucopyranoside and an 11.6% yield of methyl 6-deoxy-α-D-gluco-heptopyranoside. It can be seen from these results that when methyl 6-deoxy-6-iodo-α-D-glucopyranoside is photolysed with formaldehyde the yield of both methyl 6-deoxy-α-D-glucopyranoside, III, and methyl 6-deoxy-α-D-gluco-heptopyranoside, XXI, increases with increasing concentration of formaldehyde.



III XXI

As well as the mechanism involving addition of a radical to the carbon-oxygen double bond of formaldehyde, the following mechanisms would account for the formation of methyl 6-deoxy-α-D-gluco-heptopyranoside, XXI.

$$R\cdot + HOCH_2OCH_2OH \longrightarrow RH + HO\dot{C}HOCH_2OH \longrightarrow HCO_2H + \cdot CH_2OH$$



However, no evidence was obtained to indicate which of these possible mechanisms was the actual route of the reaction.

A solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside, buffered with sodium bicarbonate, was photolysed in the presence of a fifty molar excess of acetaldehyde. The p.m.r. spectrum of the syrup obtained when the photolysed solution was concentrated *in vacuo* showed the main product to be methyl 6-deoxy-α-D-glucopyranoside. By the use of a Celite column it was possible to separate two compounds other than starting material from the reaction mixture. These were methyl 6-deoxy-α-D-glucopyranoside (yield 79%) and methyl

FIG. 27. P.m.r. spectrum (60 Mc.p.s.) of methyl 6,8-dideoxy-D(and L)-glycero-α-D-gluco-octopyranoside (XXV) (deuterium oxide)

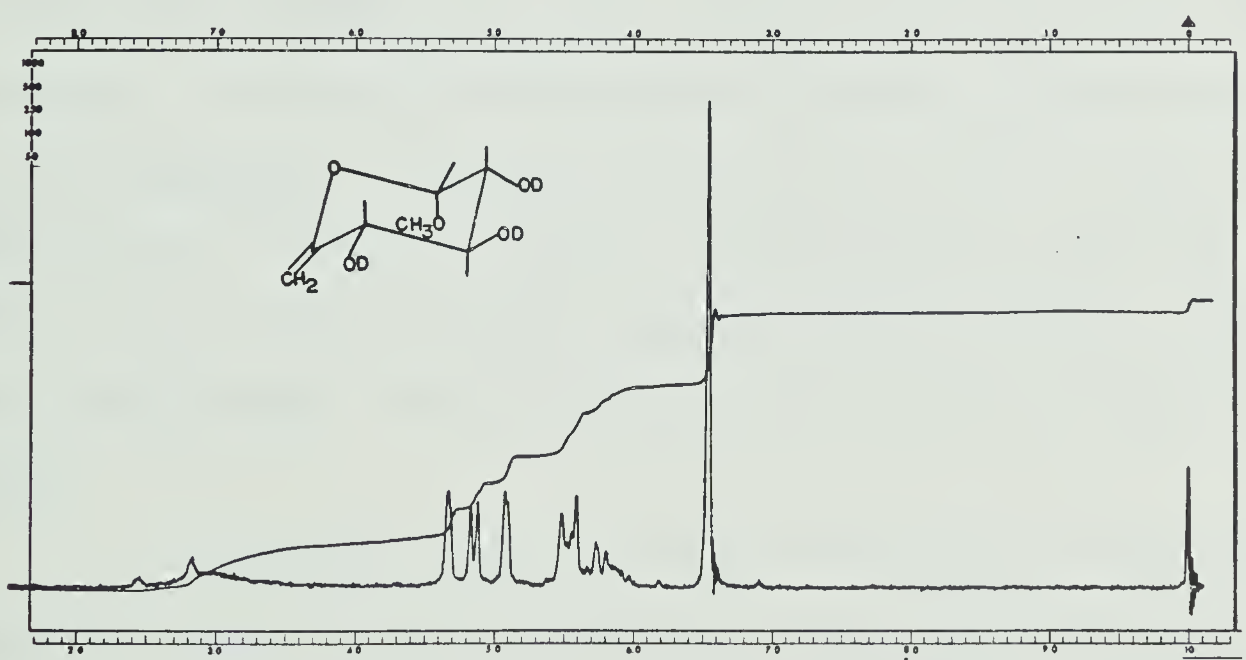


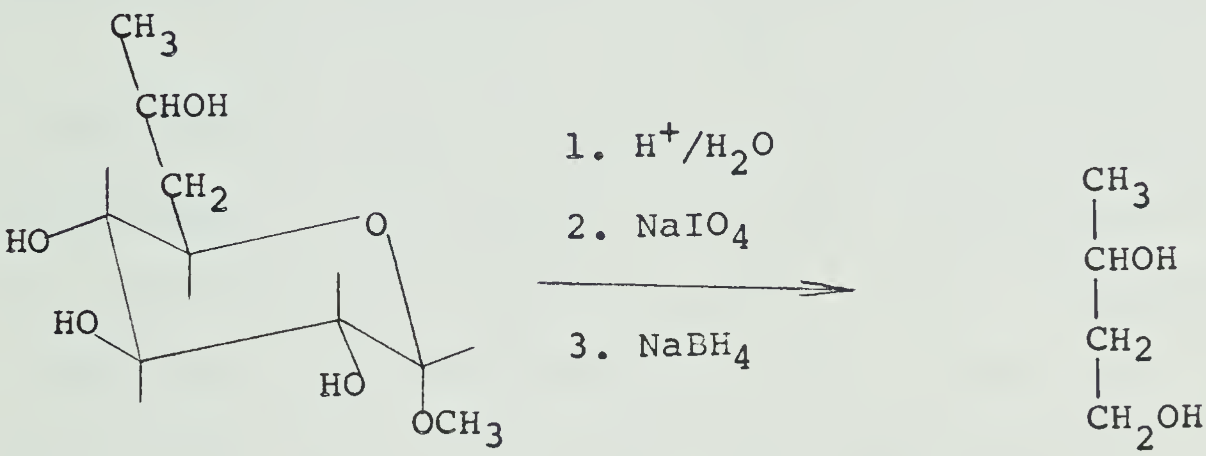
FIG. 28. P.m.r. spectrum (60 Mc.p.s.) of methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside (XIX) (deuteriopyridine)

6,8-dideoxy-D(and L)-glycero-α-D-gluco-octopyranoside, XXV, (yield 6.3%).

Support for the structure methyl 6,8-dideoxy-D (and L)-glycero-α-D-gluco-octopyranoside postulated for XXV was obtained by measuring its p.m.r. spectrum (Fig. 27) in deuterium oxide. Irradiation of the sample at 6.05τ ($H_{7,7}$) caused a partial decoupling of the multiplet in the region 8.0 - 8.3τ ($H_{6,6'}$) together with the collapse of the doublet at 8.76τ to a singlet ($H_{8,8,8}$). When the p.m.r. spectrum of XXV was measured in deuteriopyridine a triplet was obtained for the anomeric hydrogen at 5.0τ, two singlets were observed at 6.61 and 6.65τ instead of the single methoxyl singlet expected and, instead of the doublet expected for the C-methyl group, two doublets of equal intensity centred at 8.60 and 8.62τ were obtained. The most likely explanation for these results is that in the formation of methyl 6,8-dideoxy-D (and L)-glycero-α-D-gluco-octopyranoside the two possible epimers are formed at carbon-7. This would be expected since there is no apparent reason why the radical should add to the acetaldehyde carbonyl group preferentially on one particular side.

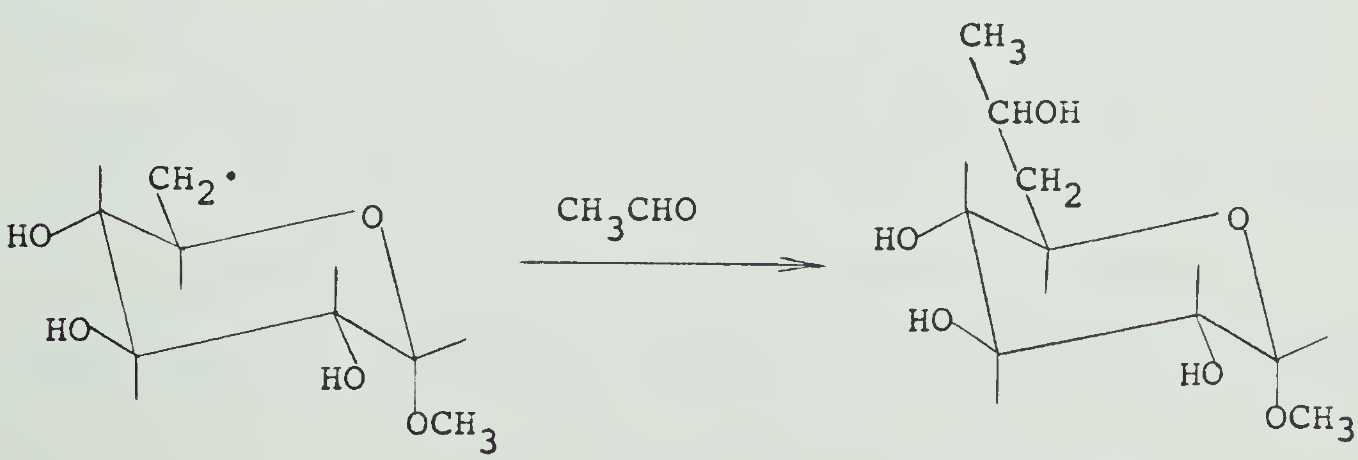
A chemical proof as to the structure of the side chain in methyl 6,8-dideoxy-D(and L)-glycero-α-D-gluco-octopyranoside was obtained by degrading the compound. An aqueous solution of methyl 6,8-dideoxy-D(and L)-glycero-α-D-gluco-octopyranoside was heated with Amberlite IR 120 (H^+)

resin to hydrolyse the methyl glycoside group. The residue was oxidized with an excess of sodium periodate and the resulting aldehyde reduced with sodium borohydride to give a syrup, XXVI, whose p.m.r. spectrum was identical to the p.m.r. spectrum of 1,3-butanediol.



XXV XXVI

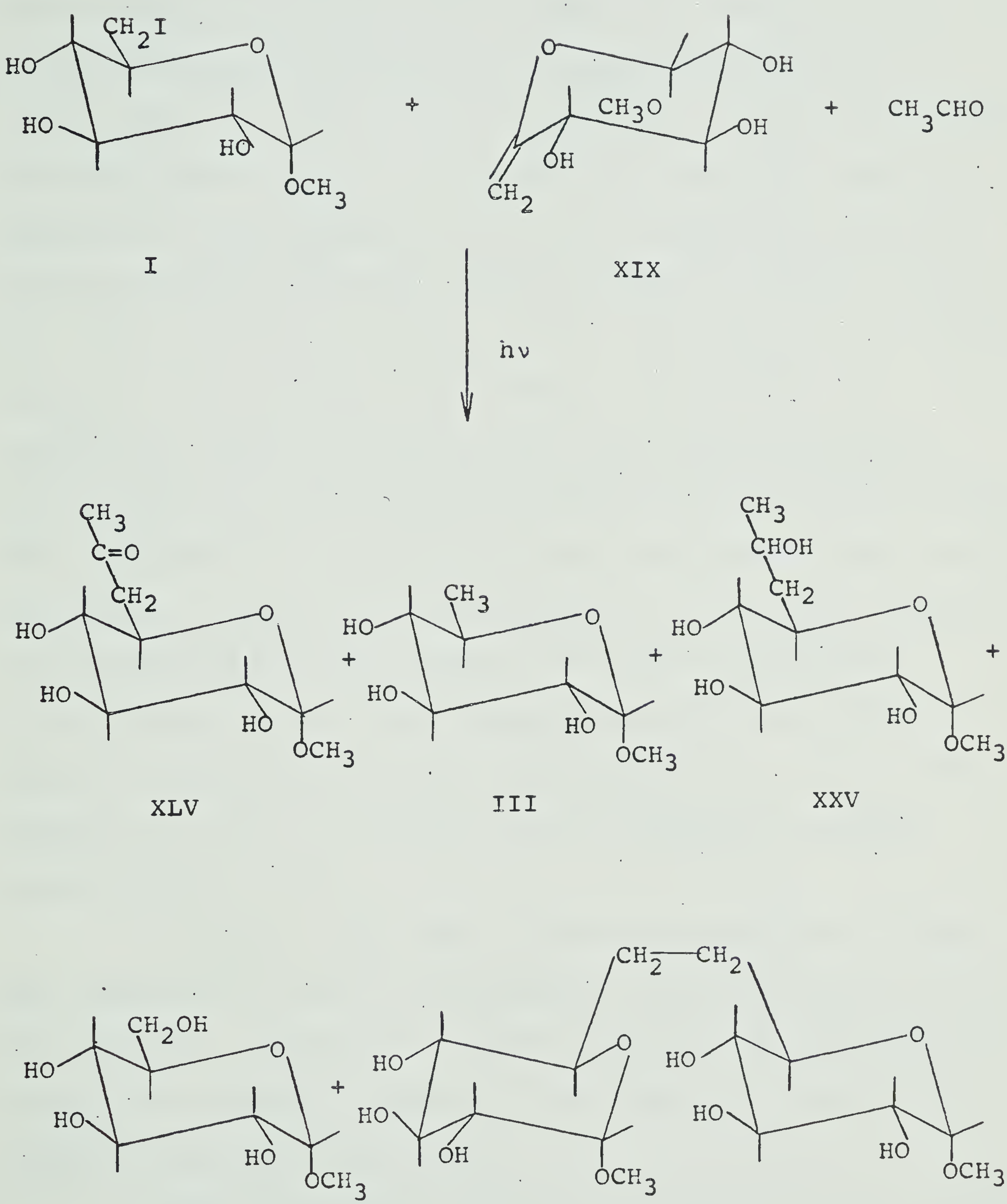
Although no evidence was obtained for the <u>gluco</u> configuration assigned to methyl 6,8-dideoxy-D(and L)-<u>glycero</u>-α-D-<u>gluco</u>-octopyranoside it would seem unlikely that any change in the configuration of the ring protons would occur during the addition of the methyl 6-deoxy-α-D-glucopyranoside radical to acetaldehyde.



II XXV

It is apparent from the high yield of methyl 6-deoxy-α-D-glucopyranoside, 79%, that the methyl 6-deoxy-α-D-glucopyranoside radical is abstracting a hydrogen atom from an acetaldehyde molecule rather than from a carbohydrate molecule when methyl 6-deoxy-6-iodo-α-D-glucopyranoside is photolysed in the presence of a large excess of acetaldehyde.

In view of the fact that none of the dimer, V, was isolated when methyl 6-deoxy-6-iodo-α-D-glucopyranoside was photolysed in the presence of either formaldehyde or acetaldehyde it was decided to attempt to gain further evidence for the mechanism involving addition of the radical, II, to the enol ether, XIX, to give the dimer radical, XX. A solution, 0.06 M in methyl 6-deoxy-6-iodo-α-D-glucopyranoside, I, 0.06 M in methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside, XIX, 6.0 M in acetaldehyde, and buffered with sodium bicarbonate was photolysed for eight hours. Separation of the photolysis mixture on a Celite column gave a major peak containing partially separated methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside, XIX, (∿50% recovered), methyl 6-deoxy-α-D-glucopyranoside, III, (yield ∿70%, based on compound I), methyl 6,8-dideoxy-α-D-*gluco*-octopyranosid-7-ulose, XLV, (yield ∿35%, based on the quantity of XIX added to the reaction mixture), methyl 6,8-dideoxy-D(and L)-*glycero*-α-D-*gluco*-octopyranoside, XXV, (yield ∿7%, based on compound I). These yields were determined by integration of the p.m.r. spectrum of the mixture. Acetylation of a portion of the mixture followed by separation



I XIX

XLV III XXV

V

of the product by chromatography on a column of silicic acid eluted with chloroform gave a fraction which crystallised from n-propanol and was shown to have the structure methyl 2,3,4-tri-O-acetyl-6,8-dideoxy-α-D-gluco-octopyranosid-7-ulose, XLVI. The methyl 2,3,4-tri-O-acetyl-α-D-glucopyranoside configuration of XLVI was apparent from the p.m.r. spectrum measured in deuteriochloroform (Fig. 29) which analysed for protons with the following chemical shifts (τ value): H_1, H_2, H_4, 5.04 - 5.26; H_3, 4.52; H_5, 5.52 - 5.76; $H_{6,6'}$, 7.1 - 7.64; $H_{8,8,8'}$ 7.79; methoxyl, 6.53; acetyl, 7.90, 7.94, 7.97. Decoupling experiments showed that the signals assigned to H_3, H_4, H_5, $H_{6,6'}$ were coupled together in the expected manner. The remainder of the structure of XLV was apparent from the fact that when a mixture containing mainly XLV and methyl 6-deoxy-α-D-glucopyranoside was reduced with sodium borohydride a g.l.c. examination of the initial mixture and the reduced product (trimethylsilyl derivative) showed that XLV had been reduced to methyl 6,8-dideoxy-D(and L)-glycero-α-D-gluco-octopyranoside, XXV.

A second, minor peak, eluted from the Celite column was estimated by paper chromatography (solvent systems A and B) and its p.m.r. spectrum to contain methyl α-D-glucopyranoside (yield ∿1%, based on compound I) and dimer, V, (yield ∿1.4%, based on compounds I and XIX).

The fact that the dimer, V, was isolated when compound I was photolysed in the presence of methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside, XIX, and excess acetaldehyde, but could

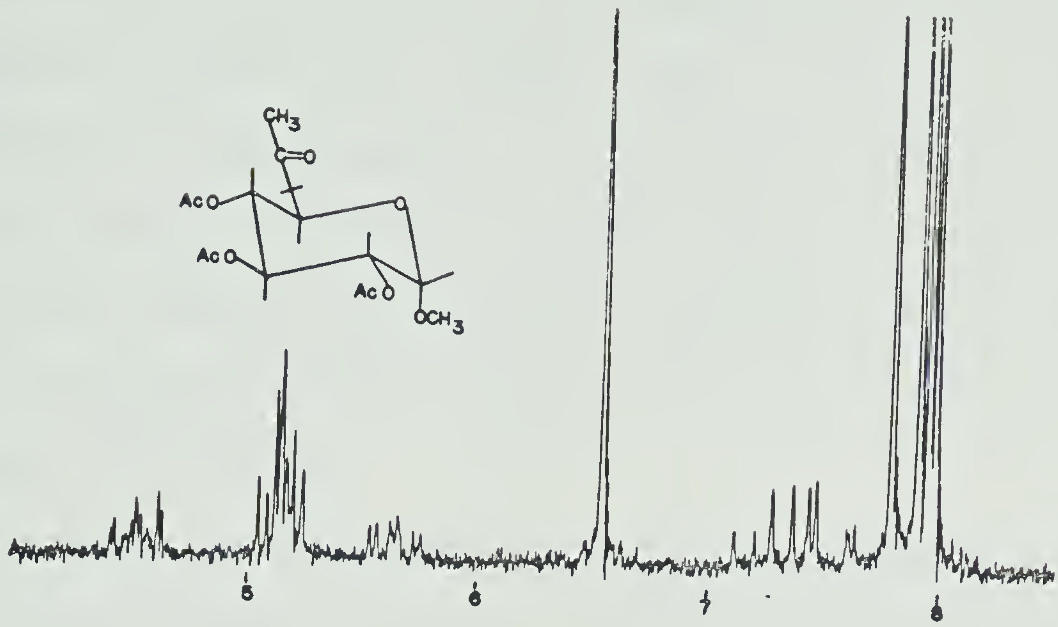


FIG. 29. P.m.r. spectrum (100 Mc.p.s.) of methyl 2,3,4-tri-O-acetyl-6,8-dideoxy-α-D-gluco-octopyranosid-7-ulose (XLVI) (deuteriochloroform)

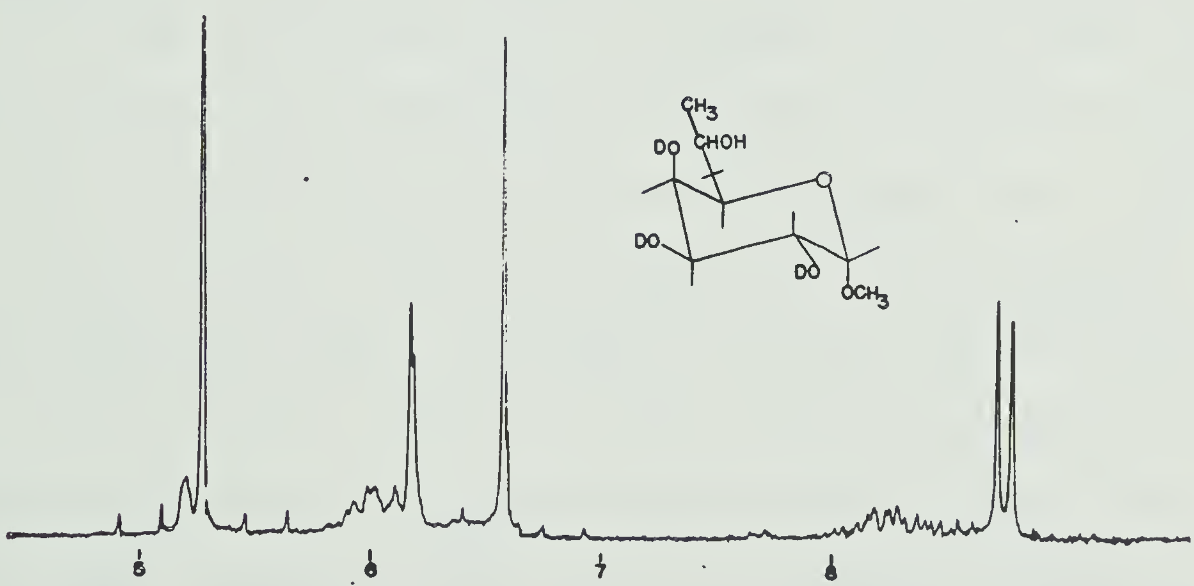
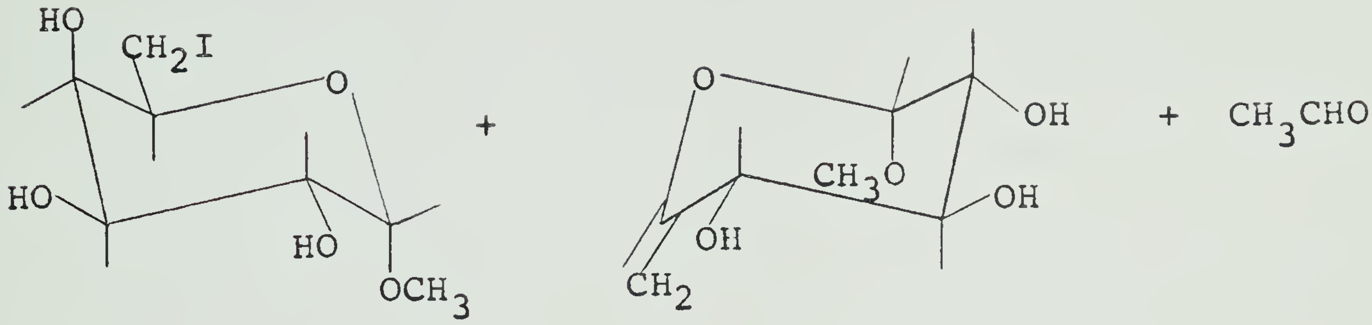


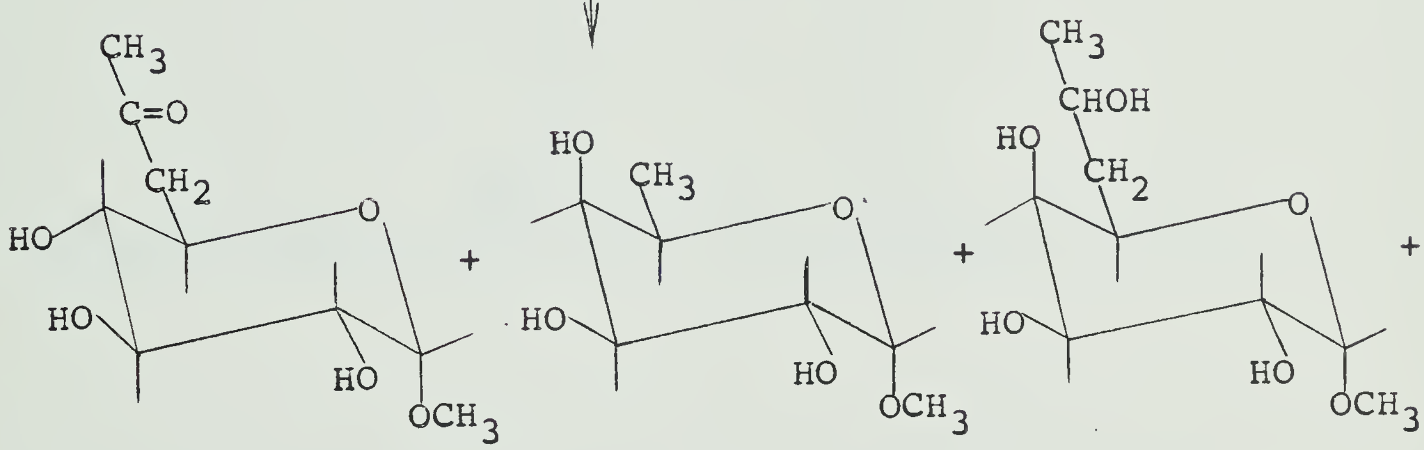
FIG. 30. P.m.r. spectrum (100 Mc.p.s.) of methyl 6,8-dideoxy-D(and L)-glycero-α-D-galacto-octopyranoside (XLVII) (deuterium oxide)

not be detected when compound I was photolysed with excess acetaldehyde (without XIX), showed that if XIX is a product of the reaction when compound I is photolysed alone, then a possible route for formation of the dimer, V, would be via the dimer radical, XX, formed by addition of the methyl 6-deoxy-α-D-glucopyranoside radical, II, to a molecule of the vinyl ether, XIX.

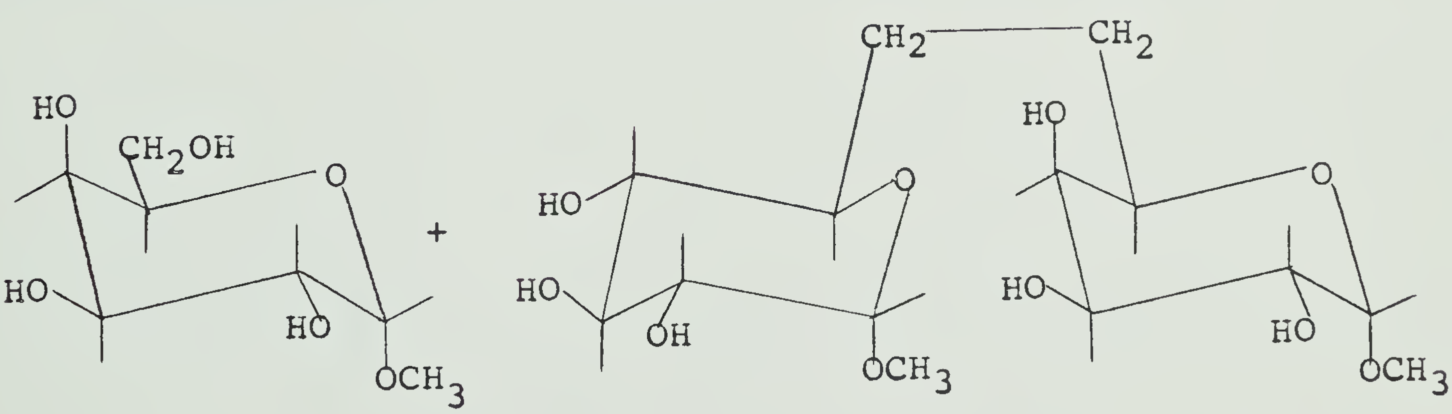
As will be described later in the Discussion it was found that when methyl 6-deoxy-6-iodo-α-D-galactopyranoside was photolysed in an aqueous solution it reacted in the same way as methyl 6-deoxy-6-iodo-α-D-glucopyranoside. It was therefore decided to photolyse methyl 6-deoxy-6-iodo-α-D-galactopyranoside, XXVII, in the presence of methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside, XIX, and excess acetaldehyde, using the same concentration of reagents and the same conditions as were used in the experiment described above with compound I. A partial separation of the photolysis product was achieved on a Celite column. The main, broad, partially separated band eluted from the column was shown to contain methyl 6-deoxy-α-D-galactopyranoside, XXVIII, (yield ~90%, based on XXVII), methyl 6,8-dideoxy-α-D-gluco-octopyranosid-7-ulose, XLV, (yield ~35%, based on XIX), methyl 6,8-dideoxy-D(and L)-glycero-α-D-galacto-octopyranoside, XLVII, (yield ~7%, based on XXVII), together with unchanged methyl 6-deoxy-α-D-xylo-hex-5-enopyranoside, XIX, (~40% recovered). The above approximate yields were based on integrations obtained from the p.m.r. spectra of fractions containing various proportions of each compound.



XXVII XIX



XLV XXVIII XLVII



XLVIII

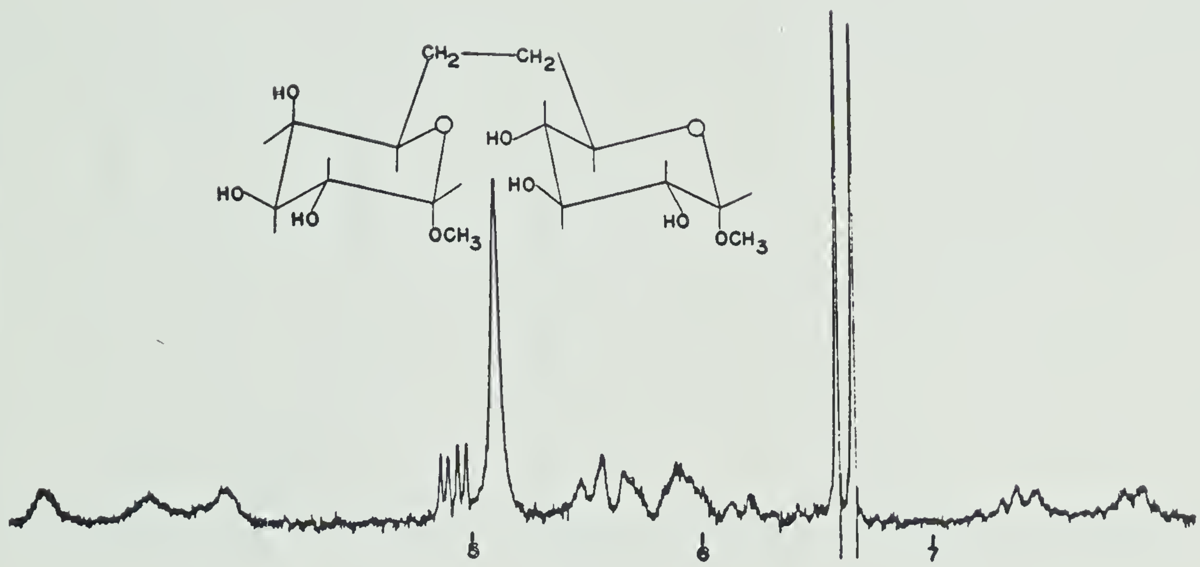


FIG. 31. P.m.r. spectrum (100 Mc.p.s.) of methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-glucopyranoside (XLVIII) (deuteriopyridine)

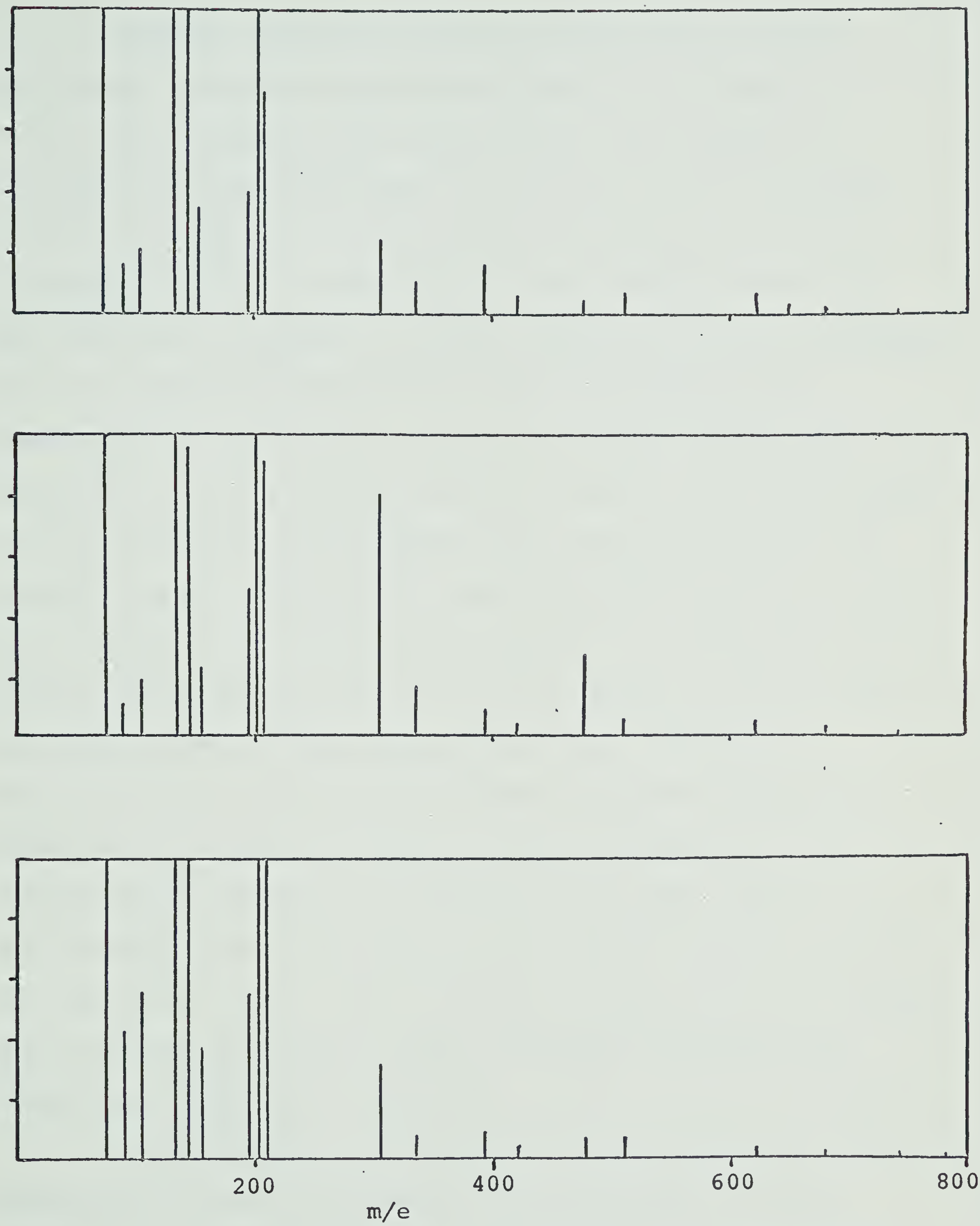


FIG. 32. Mass spectra of the trimethylsilyl derivatives of V (upper), XXXI (middle), and XLVIII (lower)

Further compounds eluted from the Celite column were methyl α-D-galactopyranoside (yield 2.7%, based on XXVII) and a compound which crystallised from methanol and was shown, as described below, to have the structure methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-glucopyranoside, XLVIII (yield 2.5%, based on XXVII and XIX). The p.m.r. spectrum of XLVIII measured in deuteriopyridine (Fig. 31) showed two doublets of equal intensity (4.88τ, spacing 3.25 c.p.s.; 4.96τ, spacing 3.5 c.p.s.) which were assigned to the two anomeric protons together with two singlets of equal intensity (6.58, 6.65τ) which were assigned to the methoxyl groups. Although the remainder of the spectrum could not be analysed as a first order spectrum it integrated for eight protons in the region 5.3 - 6.5τ (H_2-H_5, $H_{2'}$-$H_{5'}$) and for four protons in the region 7.15 - 8.0τ (-CH_2-CH_2-). Additional proof for the "mixed dimer" structure assigned to XLVIII was obtained by comparing the mass spectrum of the trimethylsilyl derivative of XLVIII to the mass spectra of the trimethylsilyl derivatives of the "glucose dimer", V, and the "galactose dimer", XXXI, as shown in Fig. 32. It was found that with the exception of small intensity differences all three mass spectra were identical.

The isolation of the "mixed dimer", XLVIII, in this experiment is positive evidence that when methyl 6-deoxy-6-iodo-α-D-galactopyranoside was photolysed in the presence of methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside, XIX, and

excess acetaldehyde the "mixed dimer", XLVIII, was formed by the addition of the methyl 6-deoxy-α-D-galactopyranoside radical to the vinyl ether, XIX, followed by hydrogen abstraction by the resulting dimer radical. These experiments demonstrate the possibility that when methyl 6-deoxy-6-iodo-α-D-glucopyranoside is photolysed, the dimer, V, arises from the addition of the methyl 6-deoxy-α-D-glucopyranoside radical, II, to methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside, XIX, produced as an intermediate in the reaction by disproportionation of II. The experiments do not rule out the possibility that the dimer, V, arises at least partially from a coupling of two methyl 6-deoxy-α-D-glucopyranoside radicals, II. An experiment which would distinguish between these two mechanisms would be the photolysis of a solution of methyl 6-deoxy-6-iodo-α-D-glucopyranoside-5-d. It is possible that if the nature or concentration of the hydrogen-atom donor used in the above experiments was changed, a sufficient quantity of the product formed by addition of the radical to the vinyl ether could be isolated to make the reaction of some use synthetically for the preparation of novel carbohydrate compounds.

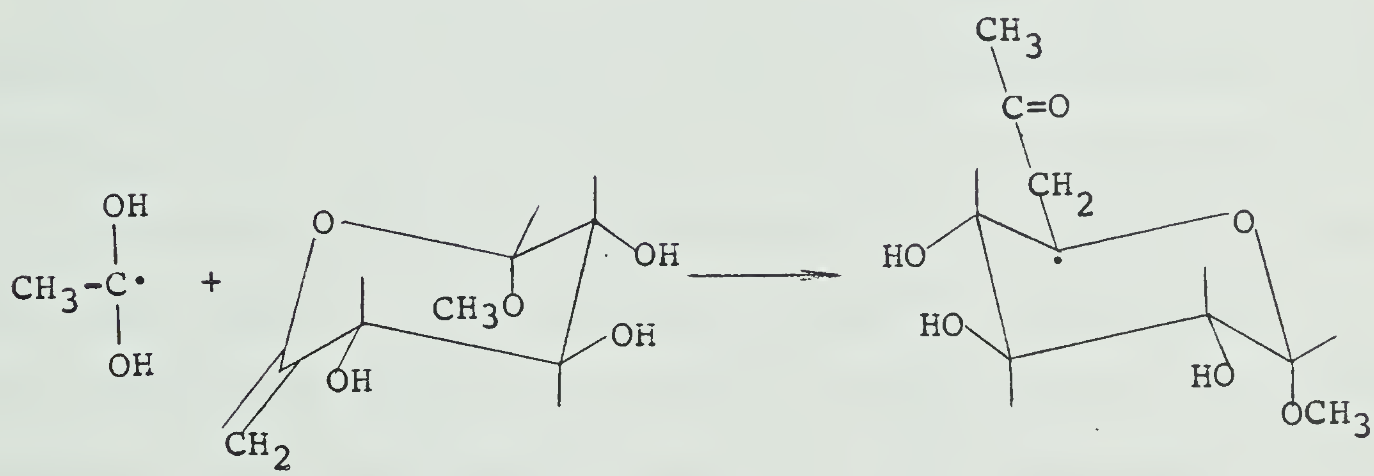
The structure of the methyl 6,8-dideoxy-D(and L)-*glycero*-α-D-*galacto*-octopyranoside, XLVII, isolated in this experiment was established by examination of its p.m.r. spectrum (Fig. 30) measured in deuterium oxide which analysed for protons with the following chemical shifts (τ value): H_1, 5.2;

H_2, H_3, H_4, H_5, H_7, 5.9 - 6.2; $H_{6,6'}$, 8.0 - 8.5; $H_{8,8,8'}$ 8.78; methoxyl, 6.57. Irradiation of the multiplet at 5.9 - 6.2τ (includes H_7) caused a partial collapse of the multiplet at 8.0 - 8.5τ ($H_{6,6'}$) and caused the doublet at 8.78τ ($H_{8,8,8}$) to collapse to a singlet. The chemical shifts of the ring protons clearly establish the galacto configuration of the compound.

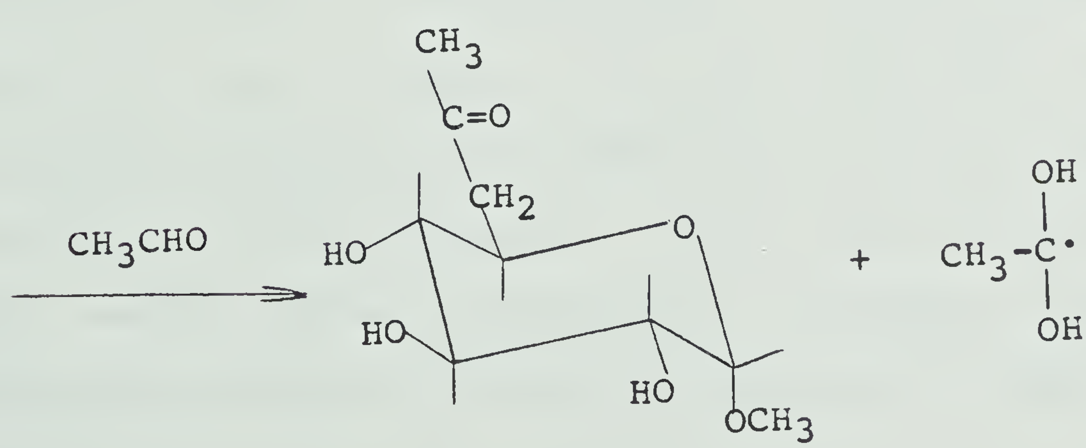
The establishment of the galacto configuration for compound XLVII clearly rules out the possibility that either it or the corresponding compound XXV in the D-gluco series could have been formed by the addition of a radical such as the $CH_3\dot{C}HOH$ radical to a vinyl ether of type XIX. The actual mechanism involved in the addition of a radical to formaldehyde or acetaldehyde in aqueous solution is difficult to formulate. It is well known that formaldehyde exists in aqueous solution almost exclusively as the hydrate, or polymer, and it is difficult to reconcile this fact with a mechanism involving addition to the carbonyl double bond of formaldehyde. A mechanism involving coupling of the $CH_3\dot{C}HOH$ radical with the methyl 6-deoxy-α-D-galactopyranoside radical seems unlikely in view of the fact that no methyl 6,8-dideoxy-D(and L)-glycero-α-D-gluco-octopyranoside, XXV, was detected in the presence of an excess of the vinyl ether, XIX. It would be expected that the radical $CH_3\dot{C}HOH$, if present, would have added to the vinyl ether XIX to give XXV.

The formation of methyl 6,8-dideoxy-α-D-gluco-

octopyranosid-7-ulose, XLV, (isolated crystalline as methyl 2,3,4-tri-*O*-acetyl-6,8-dideoxy-α-D-*gluco*-octopyranosid-7-ulose, XLVI) when methyl 6-deoxy-6-iodo-α-D-galactopyranoside was photolysed in the presence of methyl 6-deoxy-α-D-*xylo*-hex-5-enopyranoside, XIX, and excess acetaldehyde suggests that it was formed by the addition of the acetaldehyde radical to the vinyl ether, XIX, as shown below.



XIX



XLV

In order to determine whether or not the results obtained for the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside (I) were representative of other methyl 6-deoxy-6-iodo-α-D-glycopyranosides it was decided to partially repeat these experiments with methyl 6-deoxy-6-iodo-α-D-galactopyranoside which differs from compound I only in its configuration at carbon-4. Methyl 6-deoxy-6-iodo-α-D-galactopyranoside, XXVII, was prepared as described in a later section of the Discussion. Due to the limited solubility of XXVII in water all photolysis experiments were done on 0.06 M solutions of the iodo-compound.

The photolysis for seven and a half hours of a 0.06 M solution of methyl 6-deoxy-6-iodo-α-D-galactopyranoside, XXVII, buffered with sodium bicarbonate resulted in the production of sufficient acidity to neutralise about 1.4 moles of base for each mole of XXVII initially present. Chromatography of the photolysis product on a carbon-Celite column using gradient elution with ethanol-water resulted in the separation of six main peaks, labelled A, B, C, D, E, and F. Fraction A was further purified by chromatography on a microcrystalline cellulose column to give a 2.6% yield of methyl α-D-galactopyranoside. Examination of fraction B by t.l.c. showed it to consist of a single compound, XXVIII, which crystallised from ethyl acetate and was considered to be methyl 6-deoxy-α-D-galactopyranoside on the basis of its p.m.r. spectrum (Fig. 33). A doublet at 8.75τ with a spacing of 6.5 c.p.s. integrating

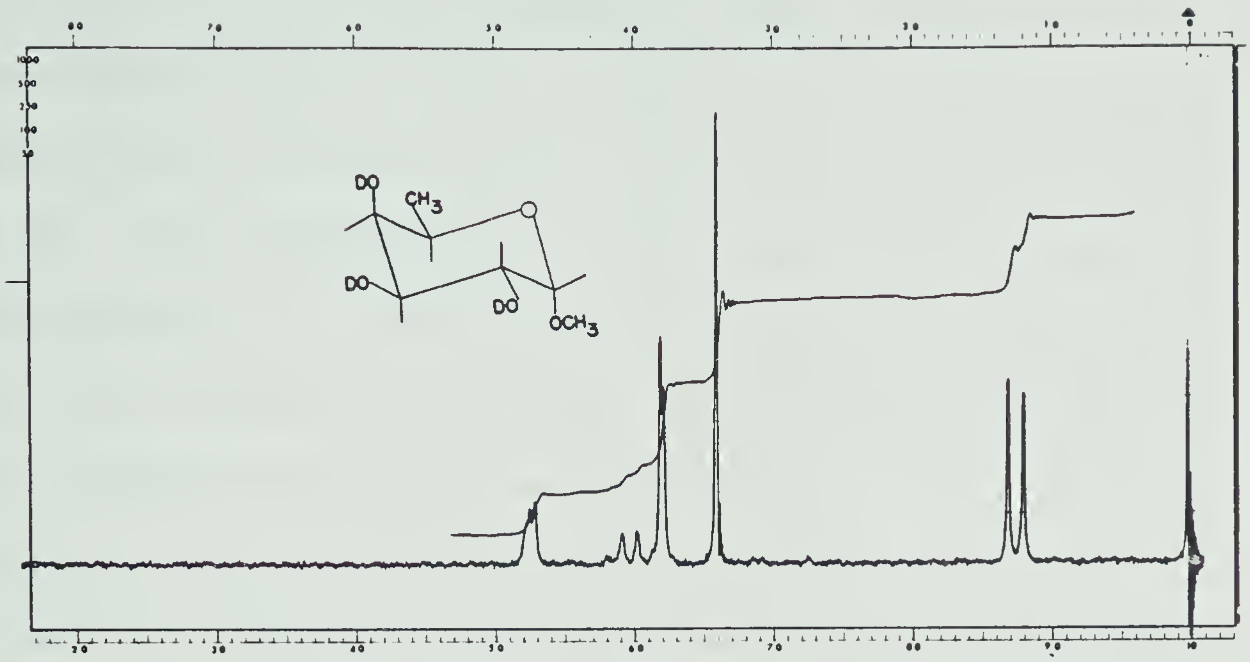


FIG. 33. P.m.r. spectrum (60 Mc.p.s.) of methyl 6-deoxy-α-D-galactopyranoside (XXVIII) (deuterium oxide)

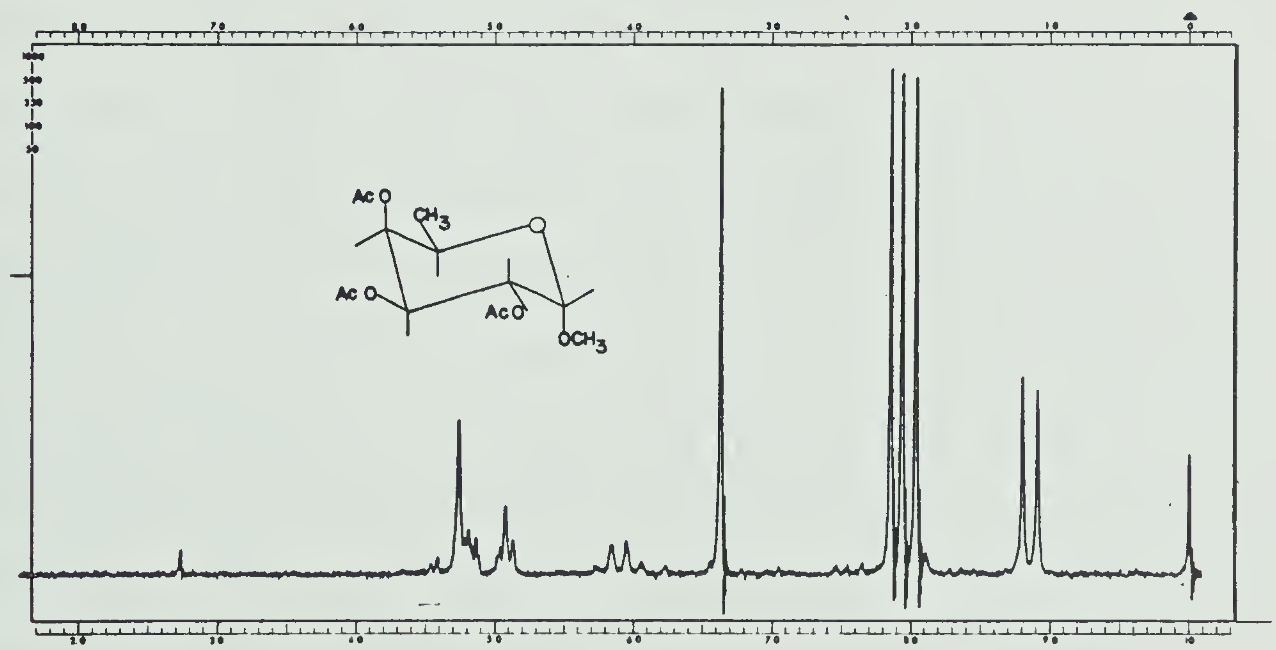


FIG. 34. P.m.r. spectrum (60 Mc.p.s.) of methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-galactopyranoside (deuteriochloroform)

for three protons was assigned to the C-methyl group ($H_{6,6,6}$). The singlet at 6.6τ was assigned to the methoxyl group and the doublet at 5.25τ with a spacing of 3.5 c.p.s. was assigned to H_1. The remainder of the spectrum, 5.75 - 6.25τ, could not be analysed as a first order spectrum, but integrated correctly for four protons, H_2, H_3, H_4, H_5. Although microanalysis of the compound gave results consistant with the molecular formula $C_7H_{14}O_5$, the physical constants ($[\alpha]_D^{25}$ +198.5° (c, 1.0 in water), m.p. 156 - 157°) were not exactly in agreement with those obtained by MacPhillamy and Elderfield (38) ($[\alpha]_D^{25}$ +190° (c, 4.1 in water), m.p. 155 - 156°) for methyl 6-deoxy-α-D-galactopyranoside; however, the physical constants do agree (opposite rotation) with those obtained by Minsaas (58) for methyl 6-deoxy-α-L-galactopyranoside. The assignment of the structure, methyl 6-deoxy-α-D-galactopyranoside is supported by the fact that acetylation with acetic anhydride in pyridine gave a crystalline compound whose p.m.r. spectrum (Fig. 34) could be explained in terms of the structure methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-galactopyranoside. Furthermore XXVIII was identical to the compound obtained by the hydrogenation of methyl 6-deoxy-6-iodo-α-D-galactopyranoside with palladium on charcoal as the catalyst. Calculating on the basis of the quantity of methyl 6-deoxy-6-iodo-α-D-galactopyranoside consumed in the reaction, the yield of methyl 6-deoxy-α-D-galactopyranoside was 23.1%.

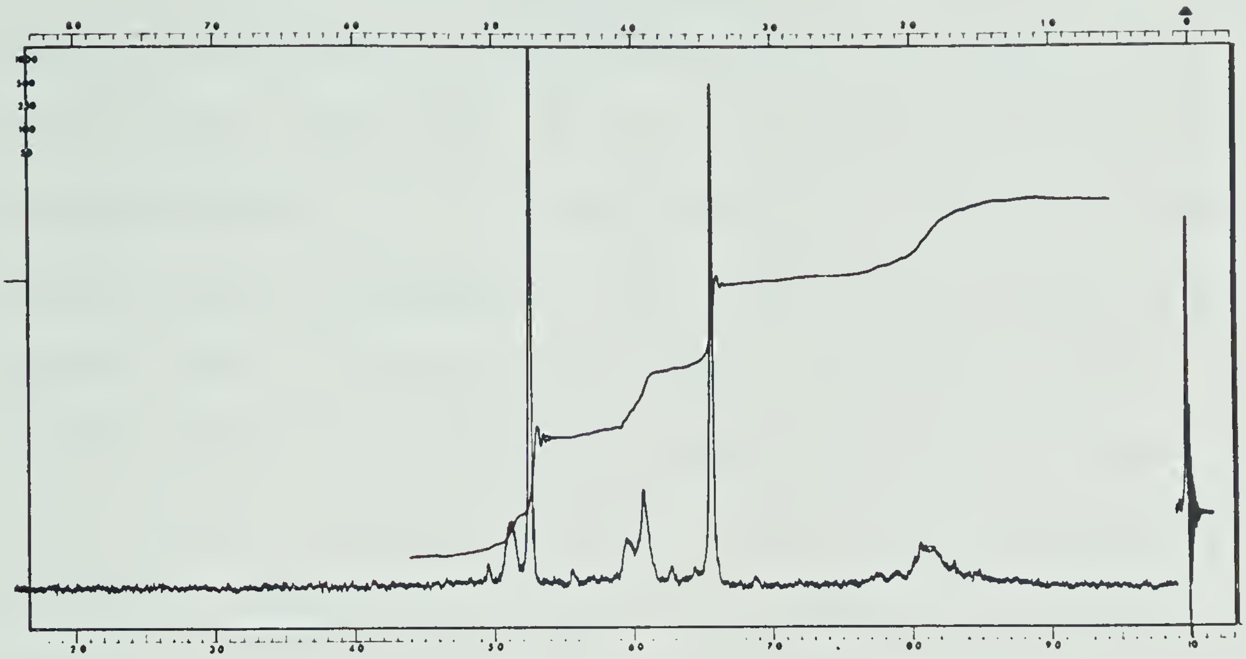


FIG. 35. P.m.r. spectrum (60 Mc.p.s.) of XXIX (deuterium oxide)

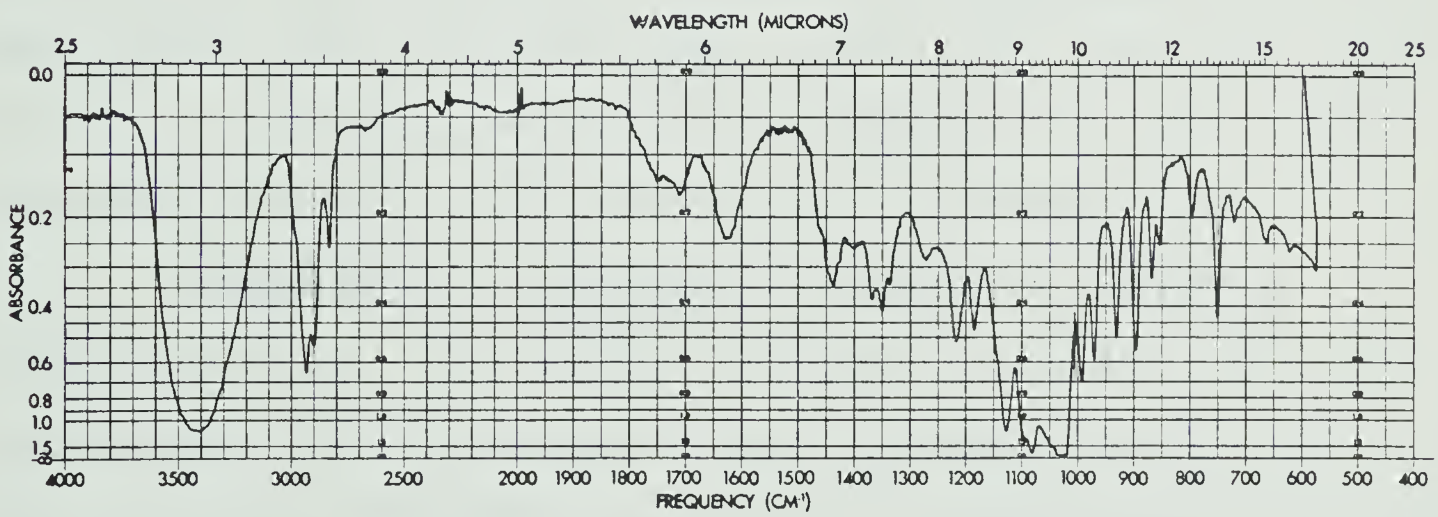
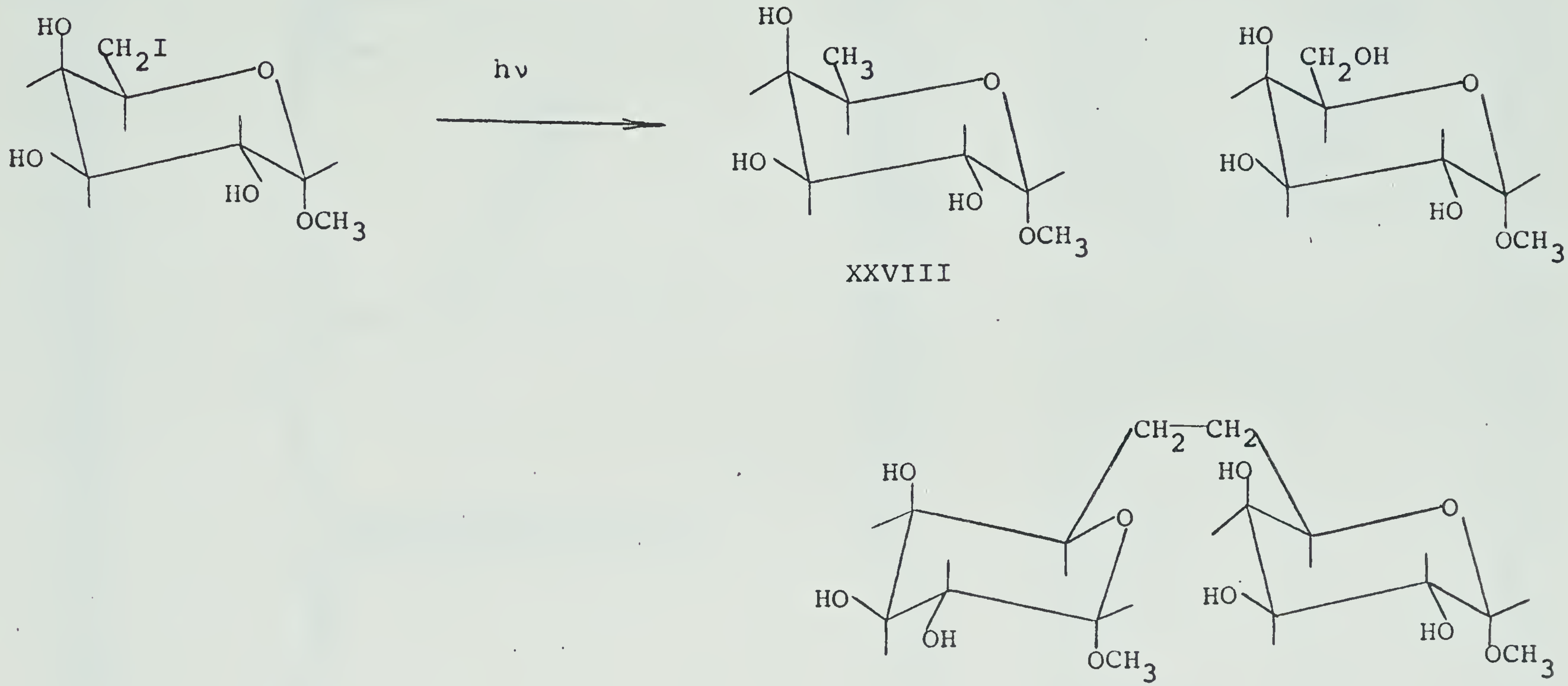


FIG. 36. I.R. spectrum (KBr disc) of XXIX

Concentration *in vacuo* of fraction C gave a syrup which crystallised on standing, but was shown by t.l.c. to contain two compounds. The two compounds were separated by chromatography on a microcrystalline cellulose column. Concentration *in vacuo* of the first peak eluted from the column gave a syrup, XXIX, which was shown by t.l.c. to consist of one compound. The p.m.r. spectrum of XXIX (Fig. 35) shows a multiplet in the region 8.0 - 8.3τ indicative of methylene protons. Examination of the I.R. spectrum of XXIX (Fig. 36) showed a strong band at 1625 cm^{-1} and a weaker band at 1710 cm^{-1}. These bands are possibly due to the presence of a carboxylic acid group (1710 cm^{-1}) and a carboxylate group (1625 cm^{-1}); possibly a mixture of the acid and its salt. No further work was done to determine the structure of XXIX in view of the small yield (~1%) obtained. Concentration *in vacuo* of the second peak eluted from the column gave a syrup, XXX, which was shown by t.l.c. to consist mainly of one compound, but with a small amount of streaking. Compound XXX was not identified.

Concentration *in vacuo* of fraction D yielded a colourless syrup which rapidly darkened on standing. The I.R. spectrum of the syrup showed a weak absorption at 1645 cm^{-1} and a stronger absorption at 1725 cm^{-1}. Examination of the syrup by t.l.c. showed at least four compounds, none of which were isolated in a pure state. However, examination of p.m.r. spectra of the partially resolved mixtures showed broad multiplets in the region 7.9τ to 8.5τ indicative of methylene protons.



XXVIII

XXXI

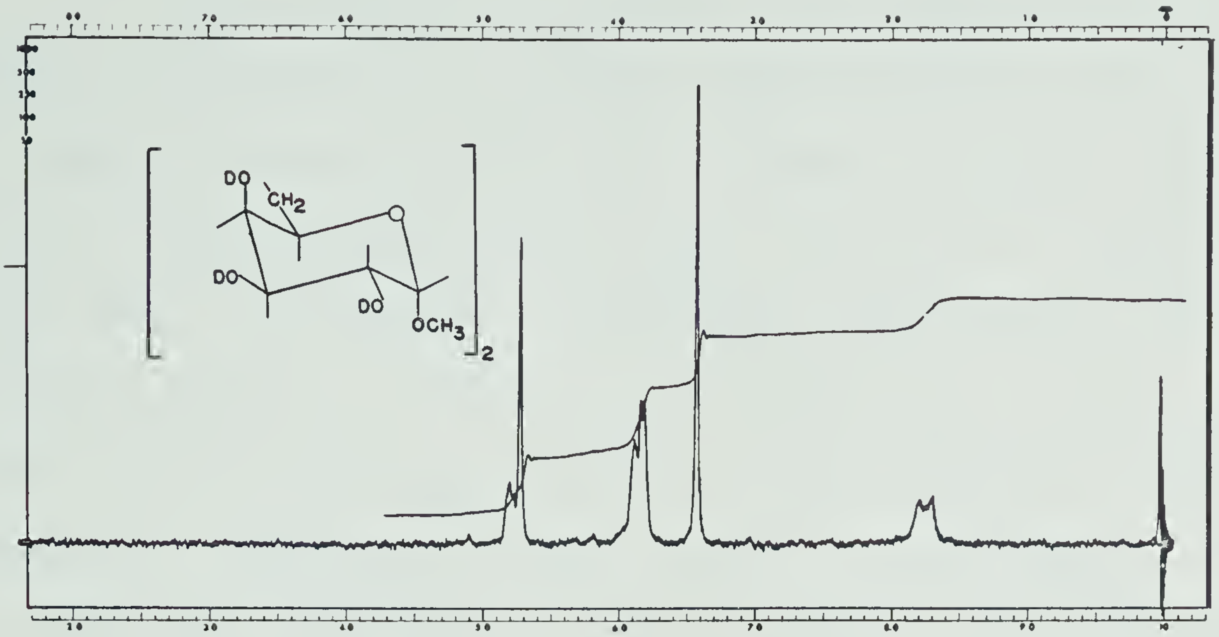


FIG. 37. P.m.r. spectrum (60 Mc.p.s.) of methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-galactopyranoside (XXXI) (deuterium oxide)

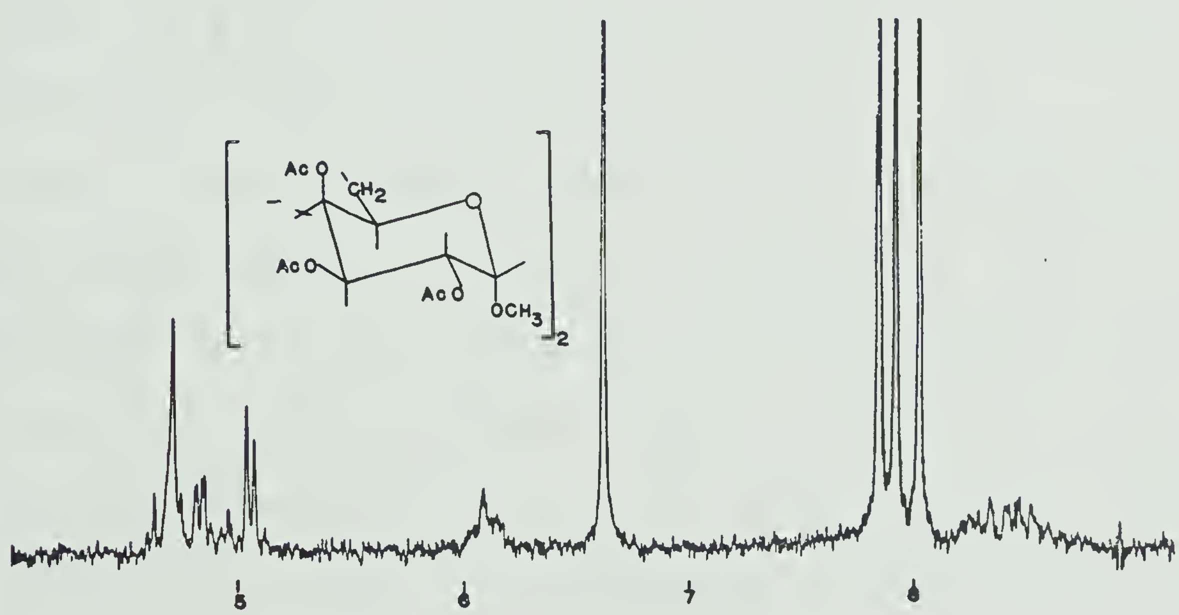


FIG. 38. P.m.r. spectrum (100 Mc.p.s.) of methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-galactopyranoside hexa-acetate (XXXII) (deuteriochloroform)

Purification of fraction E by recrystallisation gave a 6.5% yield of a compound whose structure was shown to be methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-galactopyranoside (XXXI). The p.m.r. spectrum of XXXI (Fig. 37) measured in deuterium oxide showed the following chemical shifts (τ value): H_1, 5.2 (1H); H_2, H_3, H_4, H_5, 6.05 - 6.25 (4H); $H_{6,6'}$, 8.1 - 8.4 (2H); methoxyl, 6.58 (3H). This p.m.r. spectrum is very similar in the region 5.2 - 6.3τ to the p.m.r. spectrum of methyl 6-deoxy-α-D-galactopyranoside (Fig. 33) measured in the same solvent, suggesting that the structure of XXXI is that of a dimer formed by the combination of two methyl 6-deoxy-α-D-galactopyranoside radicals. The multiplet in the region 8.1 - 8.4τ which integrated for two protons would be expected for the methylene protons ($-CH_2-CH_2-$) in such a structure. Acetylation of XXXI in a solution of pyridine and acetic anhydride gave methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-galactopyranoside hexa-acetate (XXXII). The p.m.r. spectrum of XXXII in deuteriochloroform (Fig. 38) showed the following chemical shifts (τ value): H_1, 5.06 (doublet, spacing 3.25 c.p.s.); H_2, 4.88 (octet, spacings 3.25, 1.0, 11.5 c.p.s.); H_3, H_4, 4.58 - 4.76; H_5, 6.08; $H_{6,6'}$, 8.1 - 8.7; methoxyl, 6.62; acetyl, 7.84, 7.92, 8.02.

Additional chemical proof for the dimeric structure of XXXI was obtained by oxidizing a sample of XXXI with sodium

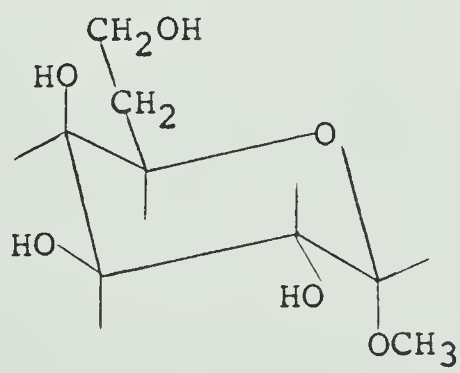
periodate, reducing the resulting aldehyde groups with sodium borohydride and hydrolysing the acetal bonds by heating the solution with Amberlite IR 120 resin (H^+). After acetylation, a syrup, XXXIII, was obtained whose p.m.r. spectrum (Fig. 39) was identical to the p.m.r. spectrum (Fig. 9) of the compound (VI) obtained by a similar degradation the "glucose dimer", V. The two compounds also displayed the same I.R. spectra and gave the same retention times when examined by gas-liquid chromatography. On this basis the structure of XXXIII is 3,4-dideoxy-tetra-O-acetyl-L-threo-hexitol, the same as the structure of VI. This result confirms the dimeric structure assigned to methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-galactopyranoside.

The last compound, fraction F, eluted from the carbon-Celite column was shown to consist of unchanged methyl 6-deoxy-6-iodo-α-D-galactopyranoside.

The yield of methyl 6-deoxy-α-D-galactopyranoside, formed by hydrogen abstraction by a methyl 6-deoxy-α-D-galactopyranoside radical, and the yield of the dimer, XXXI, are similar to the yields of methyl 6-deoxy-α-D-glucopyranoside and of the "glucose dimer", V, obtained in the photolysis of methyl 6-deoxy-6-iodo-α-D-glucopyranoside. Within experimental error the yields of the 6-deoxy compound and of the dimer are independent of the configuration of the hydroxyl at carbon-4 in the photolysis of the two iodo-glycosides.

An aqueous solution of methyl 6-deoxy-6-iodo-α-D-galactopyranoside, buffered with sodium bicarbonate, was

photolysed in the presence of a 57.6 molar excess of formaldehyde for eight hours. Aliquots, removed from the photolysis solution before and after it was photolysed, were analysed to determine the quantity of sodium bicarbonate neutralised during the reaction. For each mole of methyl 6-deoxy-6-iodo-α-D-galactopyranoside initially present in the solution, 1.33 moles of sodium bicarbonate was neutralised during the photolysis reaction. The product from the photolysis of methyl 6-deoxy-6-iodo-α-D-galactopyranoside in the presence of formaldehyde was partially separated by chromatography on a carbon-Celite column using gradient elution with ethanol-water. A complete separation of the two main products, methyl 6-deoxy-α-D-galactopyranoside, XXVIII, yield 25.8%, and methyl 6-deoxy-α-D-galacto-heptopyranoside, XXXIV, yield 19%, was achieved by chromatographing the mixture of the two on a microcrystalline cellulose column.



XXXIV

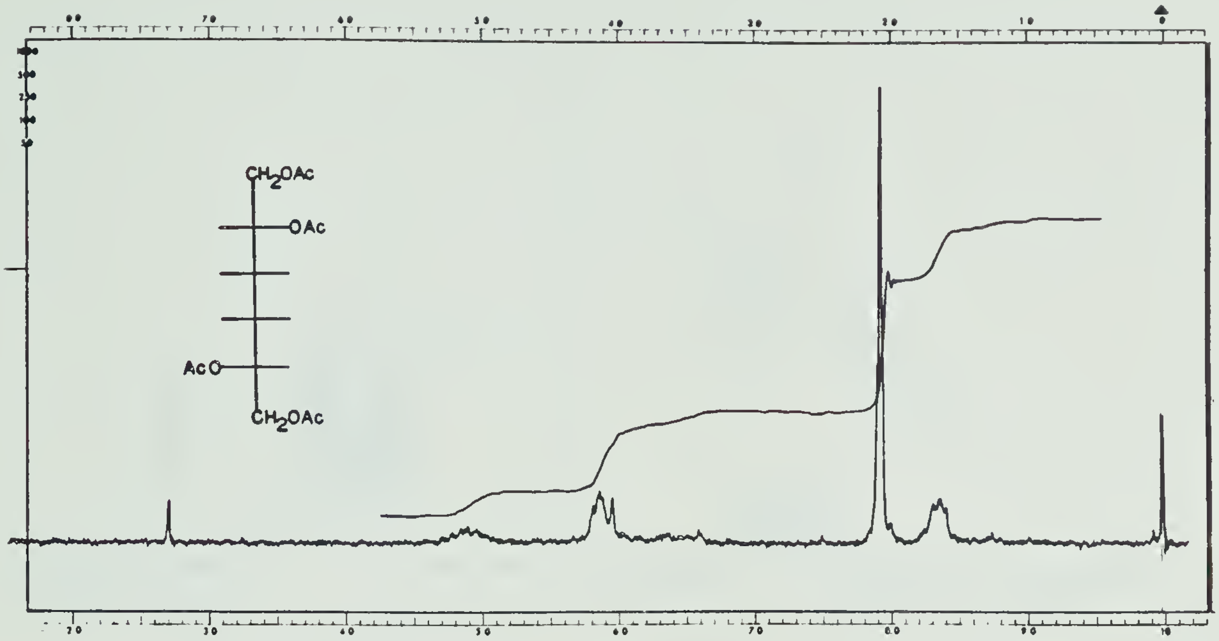


FIG. 39. P.m.r. spectrum (60 Mc.p.s.) of 3,4-dideoxy-tetra-O-acetyl-L-threo-hexitol (XXXIII) (deuteriochloroform)

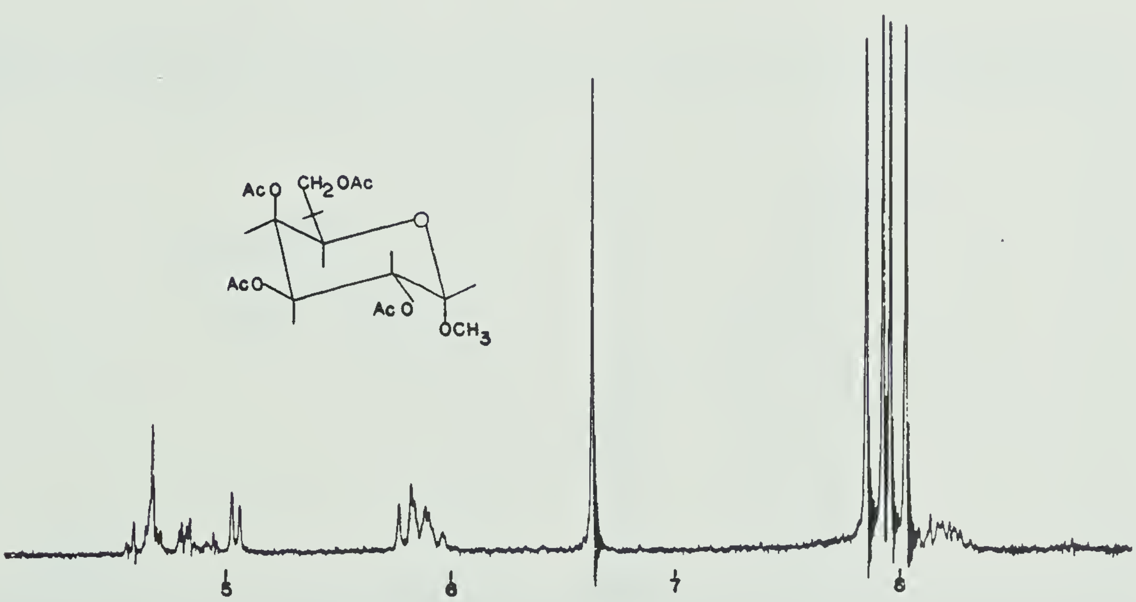


FIG. 40. P.m.r. spectrum (100 Mc.p.s.) of methyl 2,3,4,7-tetra-O-acetyl-6-deoxy-α-D-galacto-heptopyranoside (XXXV) (deuteriochloroform)

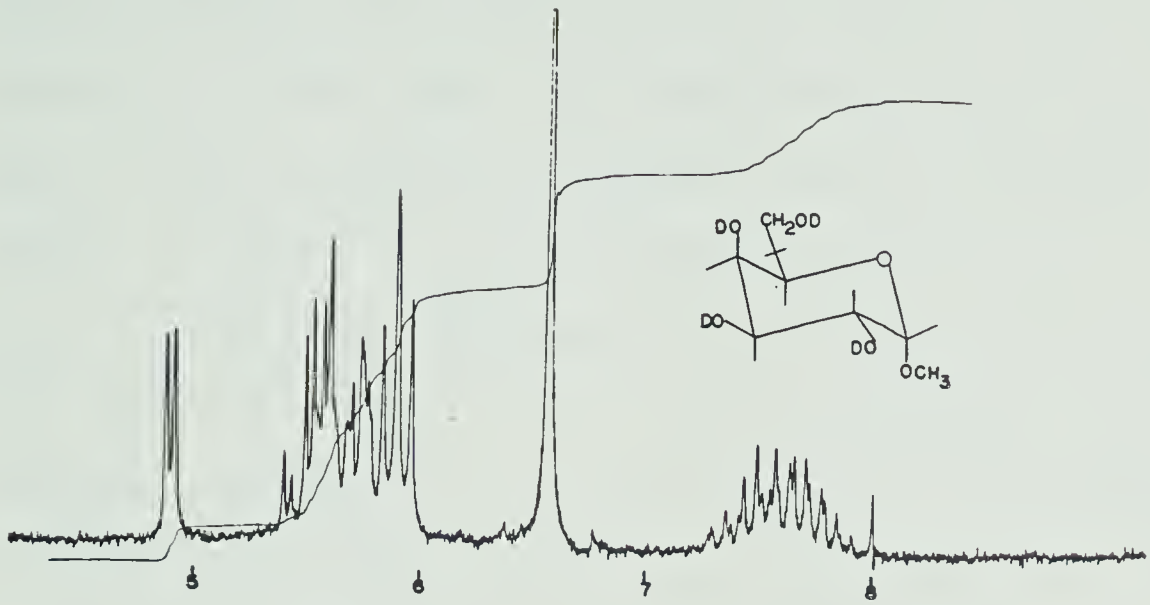


FIG. 41. P.m.r. spectrum (100 Mc.p.s.) of methyl 6-deoxy-α-D-*galacto*-heptopyranoside (XXXIV) (deuteriopyridine)

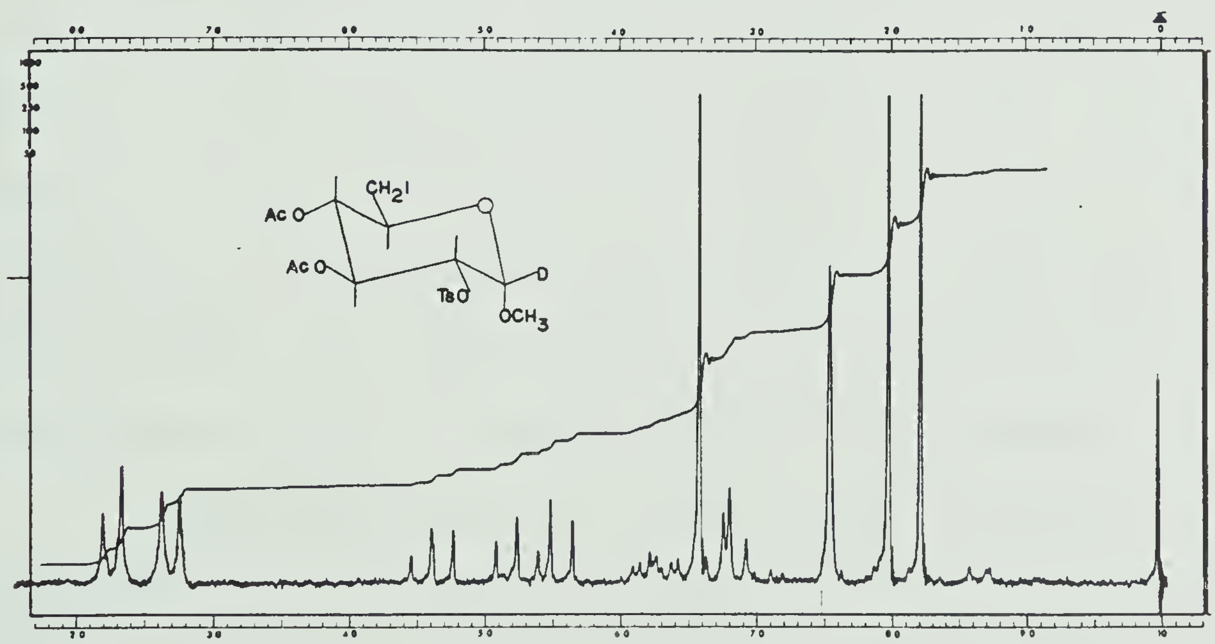


FIG. 42. P.m.r. spectrum (60 Mc.p.s.) of methyl 3,4-di-*O*-acetyl-6-deoxy-6-iodo-2-*O*-p-tolylsulfonyl-α-D-*gluco*pyranoside-1-d (XXXVII) (deuteriochloroform)

The structure, methyl 6-deoxy-α-D-galacto-heptopyranoside, was assigned on the basis of the p.m.r. spectrum of XXXIV (Fig. 41) measured in deuteriopyridine; signals were assigned to protons with the following chemical shifts (τ value): H_1, 4.90 (doublet, spacing 3.5 c.p.s.); H_2, 5.47 (quartet, spacings 3.5, 9.5 c.p.s.); H_3, H_4, H_5, 5.5 - 5.8 (3H); $H_{6,6'}$, 7.25 - 7.95 (multiplet, 2H); $H_{7,7'}$, 5.9 (triplet, spacing 6.5 c.p.s.); methoxyl, 6.57 (singlet, 3H). By the use of double irradiation experiments the following coupling constants (c.p.s.) were confirmed: $J_{1,2}$, 3.5; $J_{2,3}$, 9.5; $J_{6,7}$, 6.5. Because of the small chemical shifts between the protons H_3, H_4 and H_5 it was not possible to positively assign the signals to specific protons; however, the quartet at 5.63τ with spacings of 9.5 and 3 c.p.s. was tentatively assigned to H_3 and the quartet at 5.76τ with spacings of 3 and 1.5 c.p.s. was tentatively assigned to H_4. These couplings (c.p.s.): $J_{1,2}$, 3.5; $J_{2,3}$, 9.5; $J_{3,4}$, 3.0; $J_{4,5}$, 1.5 are of the order of the couplings which would be predicted for the ring protons of a compound with an α-D-galactopyranoside configuration from a consideration of the dihedral angles.

Additional proof for the methyl 6-deoxy-α-D-galacto-heptopyranoside structure assigned to XXXIV was obtained by acetylating XXXIV to give a compound, XXXV, whose p.m.r. spectrum (Fig. 40), measured in deuteriochloroform, was consistant with the structure methyl 2,3,4,7-tetra-O-acetyl-6-deoxy-α-D-galacto-heptopyranoside. The signals obtained were assigned

to protons with the following chemical shifts (τ value): H_1, 5.05 (doublet, spacing 3.5 c.p.s.); H_2, 4.88 (octet, spacings 12.0, 3.5 and 1.5 c.p.s.): H_3, H_4, 4.55 - 4.72; H_5, 5.89; $H_{6,6'}$, 8.05 - 8.35; $H_{7,7'}$, 5.84; methoxyl, 6.63; acetyl, 7.85, 7.93, 7.96, 8.03. As would be expected the p.m.r. spectrum of methyl 2,3,4,7-tetra-O-acetyl-6-deoxy-α-D-galacto-heptopyranoside (Fig. 40) is almost identical in the region 4.5 - 5.1τ (H_1, H_2, H_3, H_4) to the spectrum of methyl 6-deoxy-6-C-([methyl 6'-deoxy-α-D-galactopyranoside]-6-yl)-α-D-galactopyranoside hexa-acetate (Fig. 38). Decoupling experiments were done on the sample of methyl 2,3,4,7-tetra-O-acetyl-6-deoxy-α-D-galacto-heptopyranoside to show that the multiplet at 5.75 - 6.0τ (H_5, $H_{7,7}$) was coupled to the multiplet at 8.03 - 8.35τ ($H_{6,6'}$). When the mass spectrum of the trimethylsilyl derivative of methyl 6-deoxy-α-D-galacto-heptopyranoside was compared with the mass spectrum of the trimethylsilyl derivative of methyl 6-deoxy-α-D-gluco-heptopyranoside it was found that the only difference between the two were small differences in the relative intensities of various peaks. This similar fragmentation pattern for both compounds suggests that they differ only in configuration. These results suggest that the methyl 6-deoxy-α-D-galacto-pyranoside radical adds to a molecule of formaldehyde to give methyl 6-deoxy-α-D-galacto-heptopyranoside (XXXIV) in the same manner as was discussed for the methyl 6-deoxy-α-D-glucopyranoside radical.

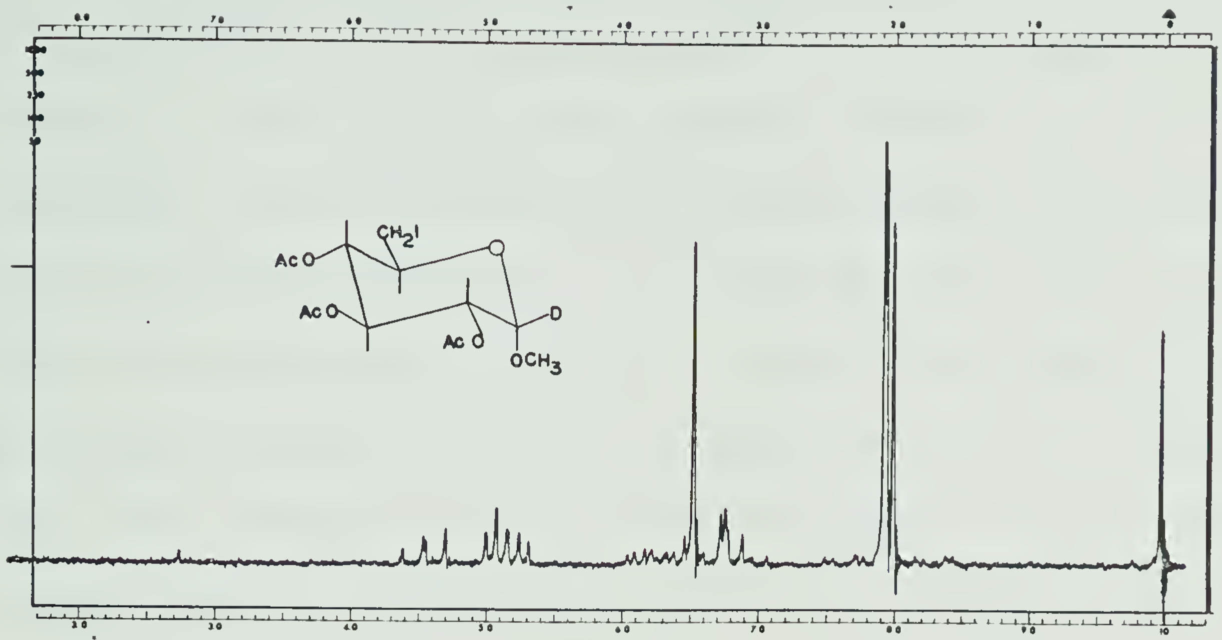


FIG. 43. P.m.r. spectrum (60 Mc.p.s.) of methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside-1-d (XXXVI) (deuteriochloroform)

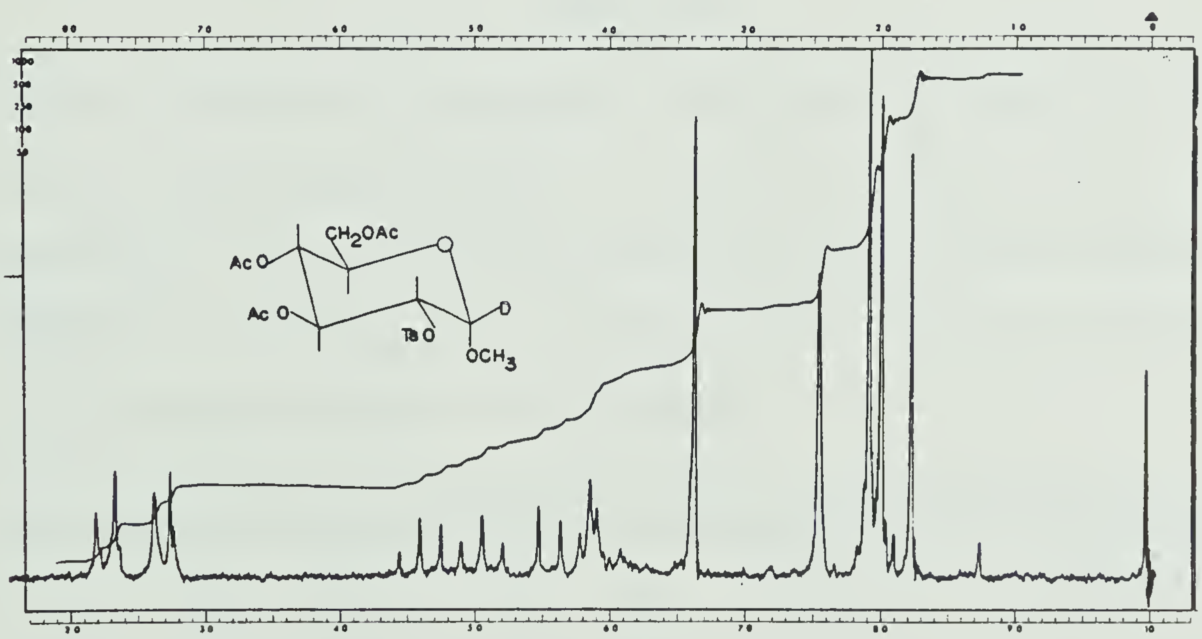


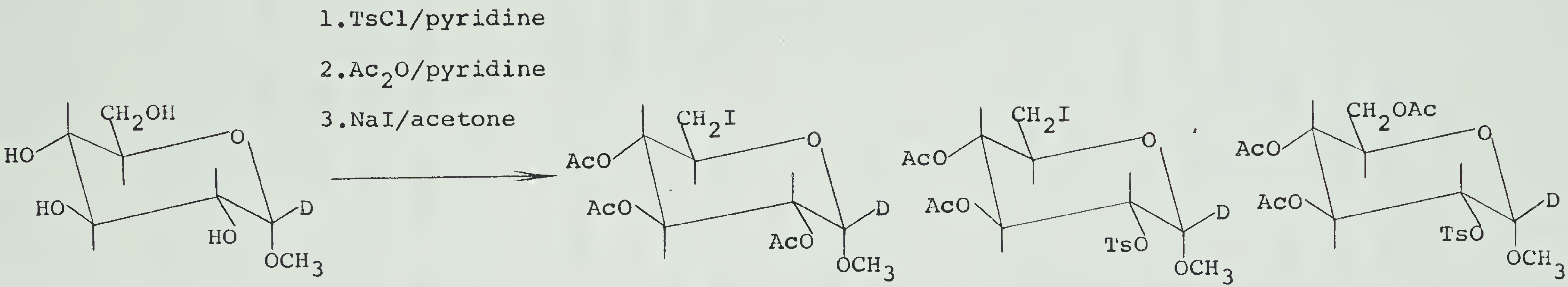
FIG. 44. P.m.r. spectrum (60 Mc.p.s.) of methyl 3,4,6-tri-O-acetyl-2-O-p-tolylsulfonyl-α-D-glucopyranoside-1-d (XXXVIII) (deuteriochloroform)

In conclusion, during the preparation of methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d (XV) and methyl 6-deoxy-6-iodo-α-D-galactopyranoside (XXVII) several other compounds were isolated due to the tosylation of methyl α-D-glucopyranoside and methyl α-D-galactopyranoside at positions other than carbon-6. The p.m.r. spectra of methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside-1-d (XXXVI) (Fig. 43), methyl 3,4-di-O-acetyl-6-deoxy-6-iodo-2-O-p-tolylsulfonyl-α-D-glucopyranoside-1-d (XXXVII) (Fig. 42), and methyl 3,4,6-tri-O-acetyl-2-O-p-tolylsulfonyl-α-D-glucopyranoside-1-d (XXXVIII) (Fig. 44) in deuteriochloroform were readily interpreted in view of the fact that replacement of H_1 by deuterium allowed the immediate assignment of the doublet to H_2.

TABLE X

P.M.R. Parameters for Methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside-1-d (XXXVI), Methyl 3,4-di-O-acetyl-6-deoxy-6-iodo-2-O-p-tolylsulfonyl-α-D-glucopyranoside-1-d (XXXVII), and Methyl 3,4,6-tri-O-acetyl-2-O-p-tolylsulfonyl-α-D-glucopyranoside-1-d (XXXVIII)

	H_2	H_3	H_4	H_5	$H_{6,6'}$	acetyl
XXXVI	5.15	4.54	5.14	6.20	6.7 - 6.9	7.92, 7.93, 7.99
XXXVII	5.57	4.61	5.23	6.26	6.73 - 6.95	7.98, 8.22
XXXVIII	5.56	4.59	5.05	6.1	5.85	7.91, 8.01, 8.22



XXXVI XXXVII XXXVIII

Protons H_3, H_4 (both triplets) and H_5 (multiplet) were assigned by reference to the results of Lemieux and Stevens (59); a partial summary of these chemical shift assignments is given in Table X (τ value). In the p.m.r. spectrum of XXXVII the doublet (5.57τ) assigned to H_2 was 0.42τ to higher field than the doublet (5.15τ) assigned to H_2 in methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside and therefore it was apparent that the structure of XXXVII was methyl 3,4-di-O-acetyl-6-deoxy-6-iodo-2-O-p-tolylsulfonyl-α-D-glucopyranoside-1-d. The high field acetyl signal at 8.22τ is attributed to an acetyl group adjacent to a p-tolylsulfonyl group (60). The chemical shift of the H_2 doublet (5.56τ) showed the structure of XXXVIII to be methyl 3,4,6-tri-O-acetyl-2-O-p-tolylsulfonyl-α-D-glucopyranoside-1-d. These results are in agreement with the previously observed reactivities of the D-glucopyranoside hydroxyl groups towards p-tolylsulfonyl chloride in pyridine. The 6-OH is the most reactive with the 2-OH more reactive than the 3-OH or the 4-OH (61).

In the preparation of methyl 6-deoxy-6-iodo-α-D-galactopyranoside (XXVII) (yield 23.4%) from methyl α-D-galactopyranoside further products were also isolated. The structure of XXVII was shown in the following manner. Since hydrogenation of XXVII gave a compound identified as methyl 6-deoxy-α-D-galactopyranoside it follows that XXVII contains a 6-deoxy-6-iodo group. The p.m.r. spectrum of methyl 6-deoxy-

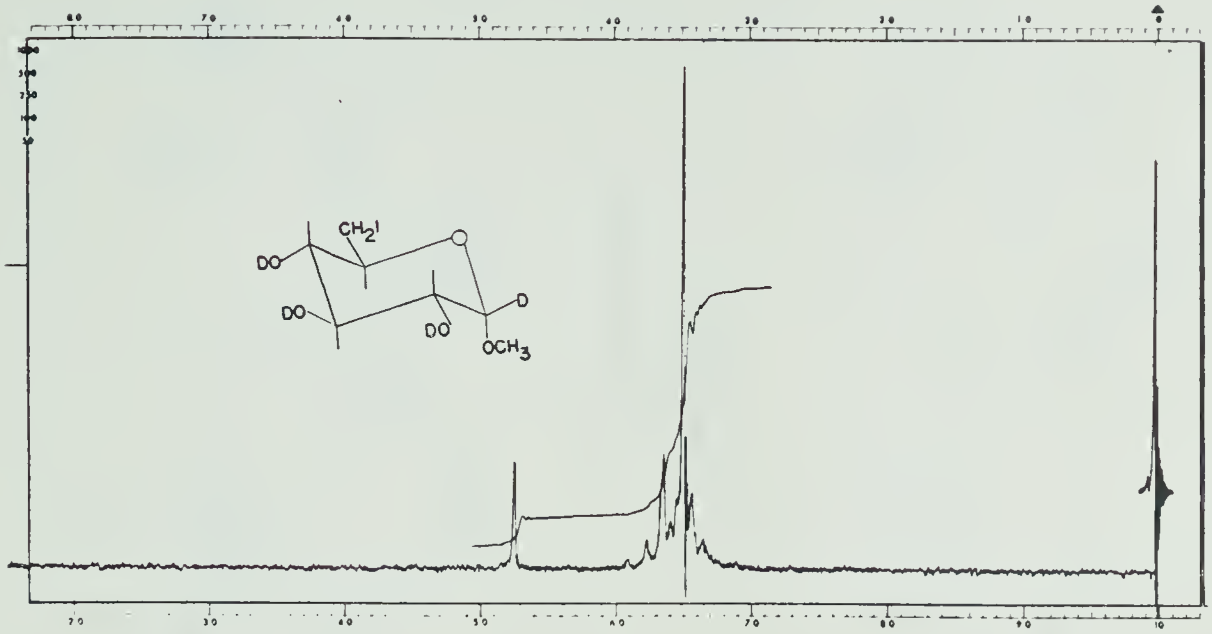


FIG. 45. P.m.r. spectrum (60 Mc.p.s.) of methyl 6-deoxy-6-iodo-α-D-glucopyranoside-1-d (XV) (deuterium oxide)

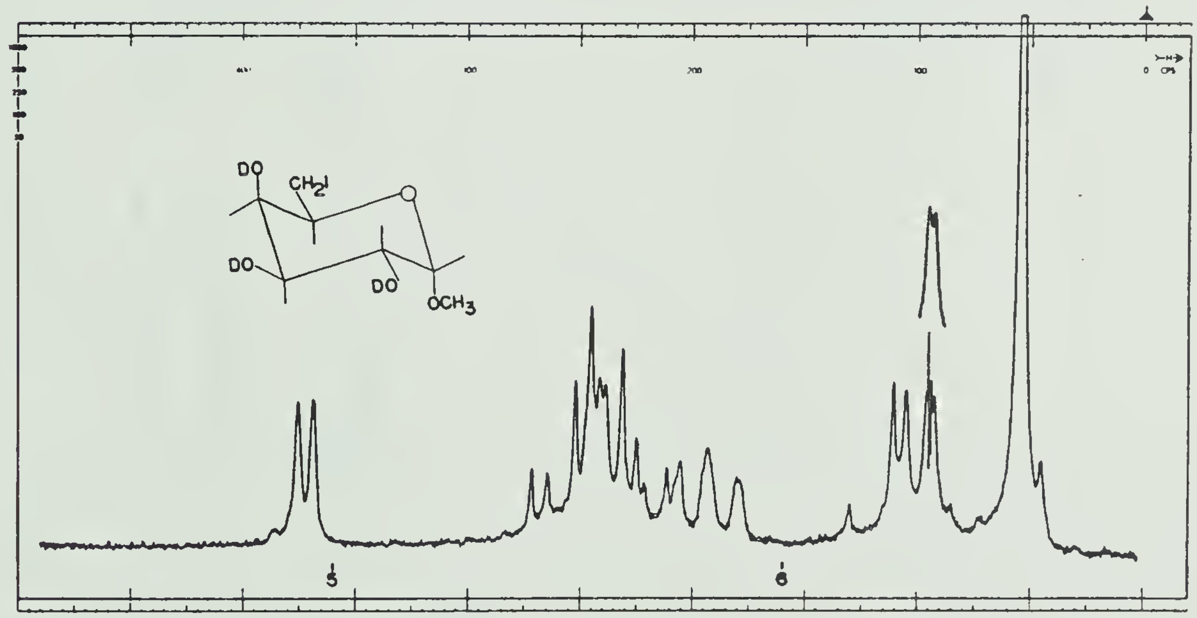
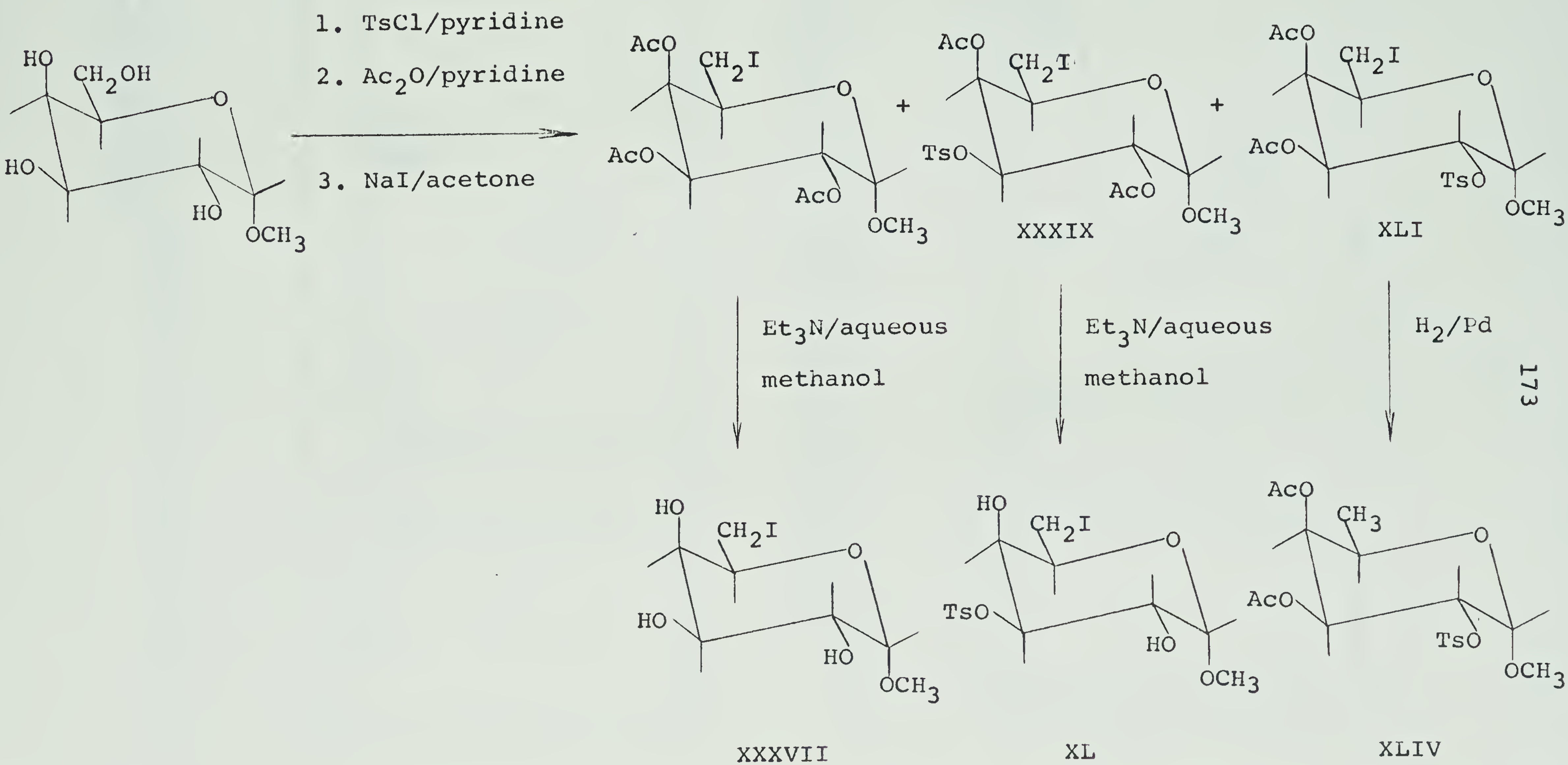


FIG. 46. P.m.r. spectrum (100 Mc.p.s.) of methyl 6-deoxy-6-iodo-α-D-galactopyranoside (XXVII) (deuteriopyridine)


1. TsCl/pyridine
2. Ac2O/pyridine
3. NaI/acetone
XXXIX
XLI
Et3N/aqueous methanol
Et3N/aqueous methanol
H2/Pd
XXXVII
XL
XLIV

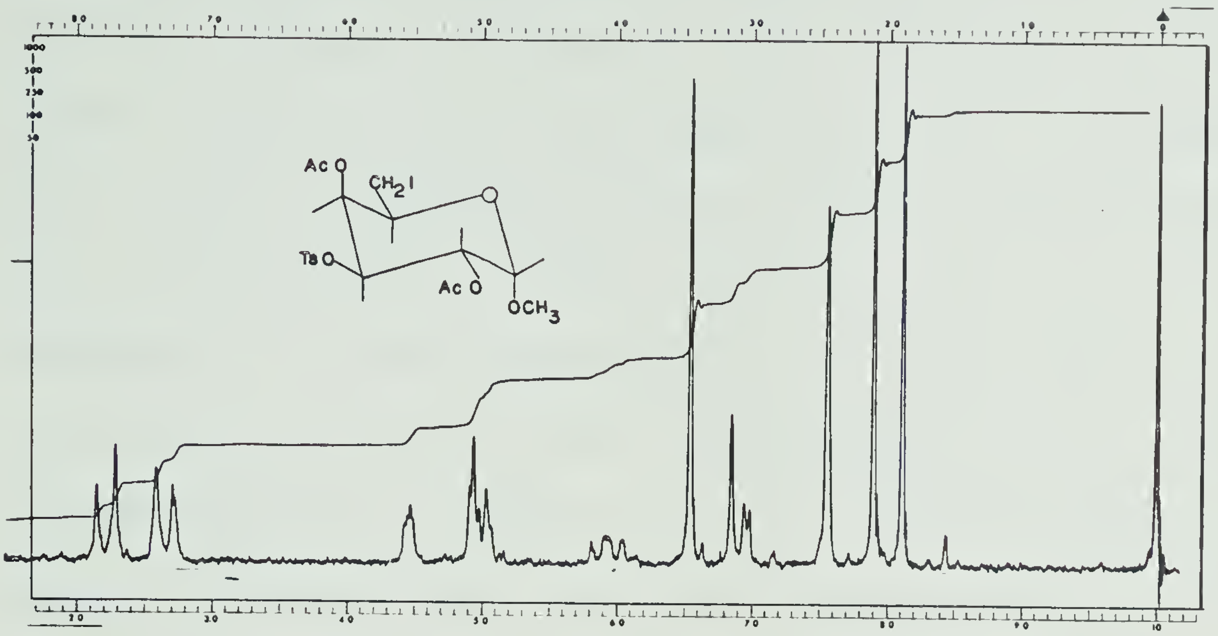


FIG. 47. P.m.r. spectrum (60 Mc.p.s.) of methyl 2,4-di-O-acetyl-6-deoxy-6-iodo-3-O-p-tolylsulfonyl-α-D-galactopyranoside (XXXIX) (deuteriochloroform)

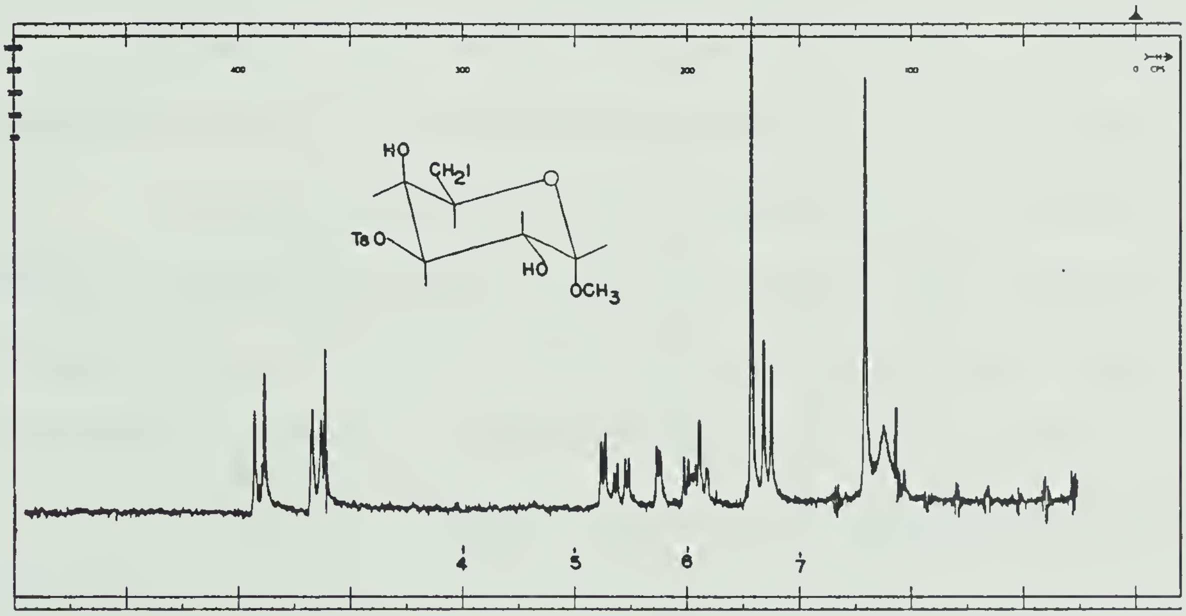


FIG. 48. P.m.r. spectrum (100 Mc.p.s.) of methyl 6-deoxy-6-iodo-3-O-p-tolylsulfonyl-α-D-galactopyranoside (XL) (deuteriochloroform)

6-iodo-α-D-galactopyranoside measured in deuteriopyridine (Fig. 46) showed a singlet at 6.54τ assigned to the methoxyl group, together with seven other protons. A multiplet at 6.26 - 6.40τ integrating for two protons was assigned to $H_{6,6'}$. The doublet at 4.94τ (spacing 3.25 c.p.s.) was assigned to H_1, and by irradiating H_1 the quartet (spacings 3.25, 9.75 c.p.s.) at 5.51τ was assigned to H_2. Irradiation of the multiplet assigned to $H_{6,6'}$ caused decoupling of the broad triplet at 5.84τ which was assigned to H_5. The quartet at 5.72τ (spacings 3.0, 9.75 c.p.s.) was assigned to H_3 on the basis of the spacings observed for H_2 which show the coupling $J_{2,3}$ to be 9.75 c.p.s. The remaining obscured narrow multiplet at approximately 5.6τ was assigned to the last proton, H_4. These observed couplings are in agreement with the couplings which would be predicted (62, 63) for methyl 6-deoxy-6-iodo-α-D-galactopyranoside in a C-1 chair conformation.

Also isolated in the preparation of XXVII was methyl 2,4-di-O-acetyl-6-deoxy-6-iodo-3-O-p-tolylsulfonyl-α-D-galactopyranoside, XXXIX, in a 2.1% yield. The p.m.r. spectrum of XXXIX in deuteriochloroform is shown in Fig. 47. It was possible to prove that the structure assigned to XXXIX was correct in the following manner. In view of the known preferential acylation of equatorial hydroxyl groups over axial hydroxyl groups (64) it was considered that methyl α-D-galactopyranoside would react preferentially with p-tolylsulfonyl chloride at carbons-2 or 3 which have equatorial

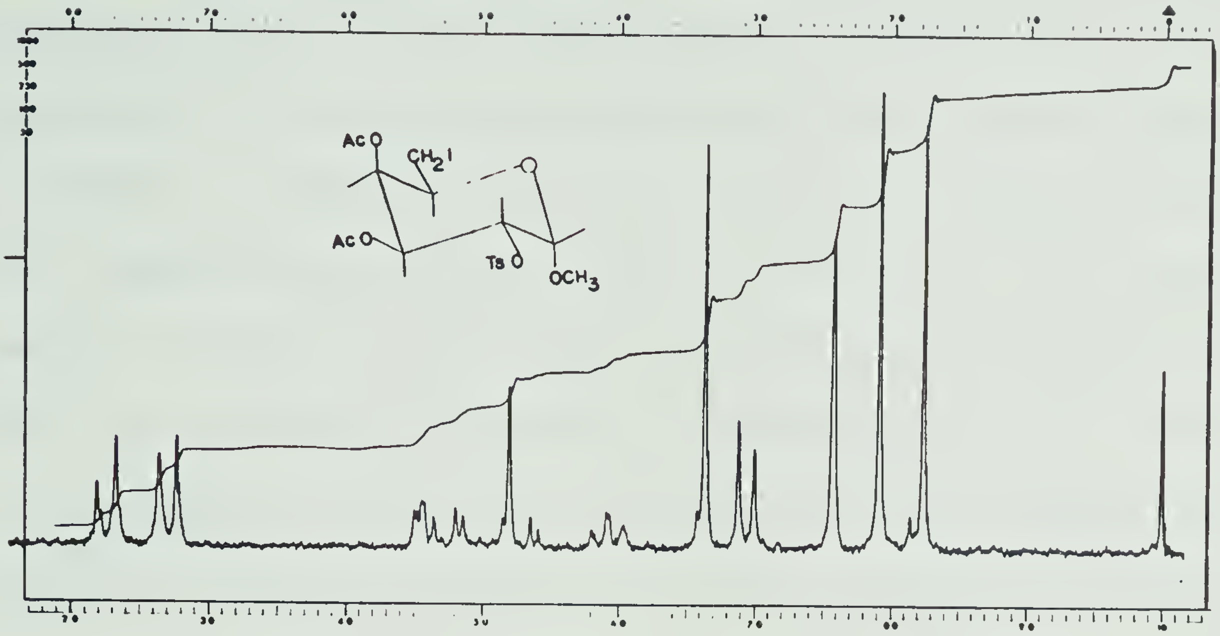


FIG. 49. P.m.r. spectrum (60 Mc.p.s.) of methyl 3,4-di-O-acetyl-6-deoxy-6-iodo-2-O-p-tolylsulfonyl-α-D-galactopyranoside (XLI) (deuteriochloroform)

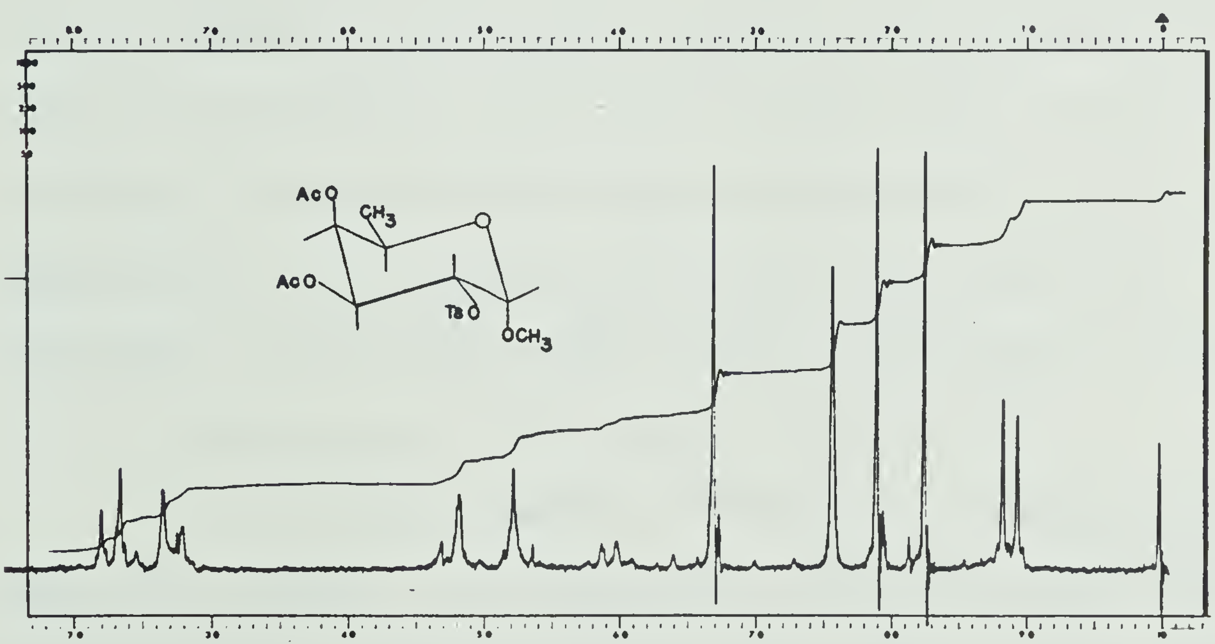


FIG. 50. P.m.r. spectrum (60 Mc.p.s.) of methyl 3,4-di-O-acetyl-6-deoxy-2-O-p-tolylsulfonyl-α-D-galactopyranoside (XLIV) (deuteriochloroform)

hydroxyl groups rather than at carbon-4 which has an axial hydroxyl group in the preferred C-1 conformation. In order to show that the O-p-tolylsulfonyl group was in fact attached to carbon-3 and not to carbon-2 compound XXXIX was deacetylated and the p.m.r. spectrum of the resulting methyl 6-deoxy-6-iodo-3-O-p-tolylsulfonyl-α-D-galactopyranoside, XL, was measured in deuteriochloroform (Fig. 48). The results of decoupling experiments allowed definite assignment of the chemical shifts of each of the ring protons (τ value): H_1, 5.25; H_2, 6.04; H_3, 5.43; H_4, 5.74; H_5, 6.1; $H_{6,6'}$, 6.71; methoxyl, 6.57; p-tolylsulfonyl, 2.18, 2.70, 7.58. Coupling constants (c.p.s.) were: $J_{1,2}$, 3.75; $J_{2,3}$, 9.75; $J_{3,4}$, 3.0; $J_{4,5}$, 1.25; $J_{5,6}$, 7.0. From the fact that the chemical shift of the H_3 proton was 0.61τ to lower field than the H_2 proton it was apparent that the H_3 proton was deshielded by the 3-O-p-tolylsulfonyl group. As a final proof of the structure of methyl 6-deoxy-6-iodo-3-O-p-tolylsulfonyl-α-D-galactopyranoside it was shown that it did not react with sodium periodate. This proves that the two free hydroxyl groups in the molecule are not vicinal to each other.

A further compound isolated in the preparation of XXVII was methyl 3,4-di-O-acetyl-6-deoxy-6-iodo-2-O-p-tolylsulfonyl-α-D-galactopyranoside (XLI) (yield 11%). The p.m.r. spectrum of XLI measured in deuteriochloroform is shown in Fig. 49. To verify that the O-p-tolylsulfonyl

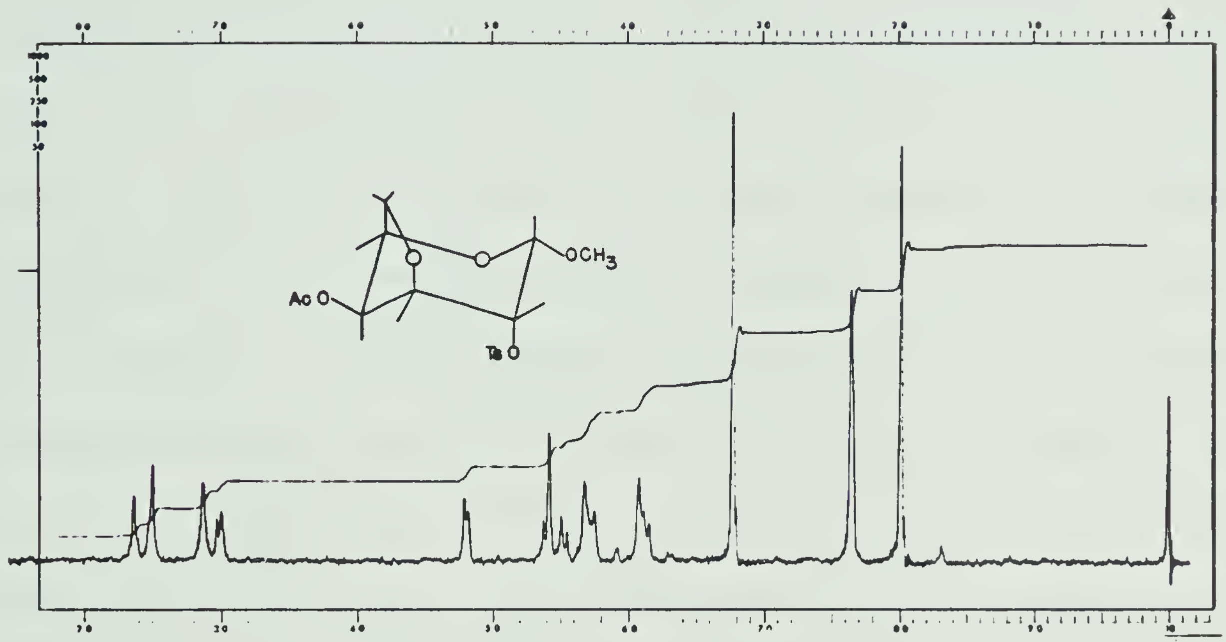


FIG. 51. P.m.r. spectrum (60 Mc.p.s.) of methyl 4-O-acetyl-3,6-anhydro-2-O-p-tolylsulfonyl-α-D-galactopyranoside (XLIII) (deuteriochloroform)

group was in fact attached to carbon-2 a portion of the methyl 3,4-di-O-acetyl-6-deoxy-6-iodo-2-O-p-tolylsulfonyl-α-D-galactopyranoside was deacetylated by dissolving it in an aqueous solution of triethylamine and methanol. The product obtained consisted of two compounds, methyl 6-deoxy-2-O-p-tolylsulfonyl-α-D-galactopyranoside and methyl 3,6-anhydro-2-O-p-tolylsulfonyl-α-D-galactopyranoside. By hydrogenation of the mixture crystalline methyl 4-O-acetyl-3,6-anhydro-2-O-p-tolylsulfonyl-α-D-galactopyranoside (XLIII) (Fig. 51) was separated from the methyl 3,4-di-O-acetyl-6-deoxy-2-O-p-tolylsulfonyl-α-D-galactopyranoside (XLIV) remaining in the mother liquor. Compound XLIV was considered to be methyl 3,4-di-O-acetyl-6-deoxy-2-O-p-tolylsulfonyl-α-D-galactopyranoside on the basis of its p.m.r. spectrum measured in deuteriochloroform (Fig. 50). The doublet at 8.88τ with a spacing of 6.5 c.p.s. was assigned to the 6-deoxy group. Integration of the singlets at 6.69, 7.56, 7.9 and 8.25τ showed the presence of a methoxyl group, a p-tolylsulfonyl group and two acetyl groups respectively. This confirms the assignment of the iodide to carbon-6. It is apparent that the conditions used for the triethylamine deacetylation of methyl 3,4-di-O-acetyl-6-deoxy-6-iodo-2-O-p-tolylsulfonyl-α-D-galactopyranoside are sufficiently basic to cause some 3,6-anhydro formation. The fact that it is possible to form the 3,6-anhydro compound is additional proof that the O-p-tolylsulfonyl group is not attached to carbon-3, but is attached to carbon-2.

Smith and coworkers (65, 66) isolated both methyl 6-O-p-tolylsulfonyl-α-D-galactopyranoside and methyl 2,6-di-O-p-tolylsulfonyl-α-D-galactopyranoside from the reaction mixture obtained when methyl α-D-galactopyranoside was treated with p-tolylsulfonyl chloride. On the other hand Reichstein and coworkers (67 - 70) obtained a preponderance of the 3-O-p-tolylsulfonyl derivative admixed with a little of the 2-O-p-tolylsulfonyl and 2,3-di-O-p-tolylsulfonyl derivatives when methyl 4,6-O-benzylidene-α-D-galactopyranoside was reacted with p-tolylsulfonyl chloride. The results obtained in this present research suggest that in the case of methyl α-D-galactopyranoside the order of reactivity of the hydroxyl groups toward p-tolylsulfonyl chloride is 6 > 2 > 3.

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